Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
This journal is © The Royal Society of Chemistry 2016

SUPPORTING INFORMATION

Title: From Acyclic to Cyclic α-Amino Vinylphosphonates by Using Ring-Closing Metathesis
Author(s): Pauline Adler, Antoine Fadel, Joëlle Prunet*, Nicolas Rabasso*

EXPERIMENTAL SECTION 1
GENERAL METHODS 1
GENERAL PROCEDURE A FOR THE PREPARATION OF THE YNAMIDES FROM THE SULFONAMIDES 1
GENERAL PROCEDURE B FOR THE PREPARATION OF THE α-AAPS FROM THE YNAMIDES 1
GENERAL PROCEDURE C FOR THE REDUCTION OF α-AAPS INTO α-AVPS 3
^{1}H AND ^{13}C NMR SPECTRA 5
SPECTRA OF THE α-AAPS 13 5
SPECTRA OF THE PMB-PROTECTED α-AVPS 14 9
SPECTRA OF THE DEPROTECTED α-AVPS 15 14
SPECTRA OF THE α-AVPS 16 22
SPECTRA OF THE PRODUCTS OF METATHESIS 39

EXPERIMENTAL SECTION

GENERAL METHODS

All reactions were carried out under argon with magnetic stirring. All solvents and chemicals were purified based on standard procedures. Reagent grade solvents were used without purification for all extractions and work-up procedures. R_f values refer to values obtained by TLC on 0.25 mm silica gel plates (60F254). Flash chromatography was carried out on silica gel 60 (15– 40 μm) with various mixtures of ethyl acetate (EtOAc) and petroleum ether (PE), yields refer to chromatographically and spectroscopically pure compounds. NMR spectra were recorded at 250, 300, 360, 400, 500 MHz. HRMS spectra were recorded with a MicroTOFq spectrometer.

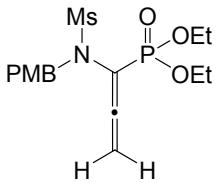
GENERAL PROCEDURE A FOR THE PREPARATION OF THE YNAMIDES FROM THE SULFONAMIDES

Sulfonamide (2.05 mmol), $CuSO_4.5H_2O$ (0.205 mmol), 1,10-phenanthroline (0.411 mmol), and K_3PO_4 (4.11 mmol) were heated to 70 °C in 2 mL of dry toluene under inert atmosphere. Bromoalkyne (2.71 mmol) in 2 mL of dry toluene was then slowly added. After 4 h at 70 °C, the mixture was cooled to room temperature, filtered through a pad of Celite, and concentrated in vacuo. Purification by flash chromatography on silica gel yielded the ynamide.

GENERAL PROCEDURE B FOR THE PREPARATION OF THE α-AAPS FROM THE YNAMIDES

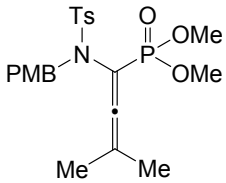
To a solution of ynamide (2.05 mmol) in 16 mL of anhydrous tetrahydrofuran cooled at 0 °C were added triethylamine (2.26 mmol) and chlorophosphite (2.26 mmol). After 18 h of stirring at room temperature, the mixture was filtered through a pad of Celite®, the solvent was removed in vacuo, and crude product was purified by flash chromatography on silica gel to yield the amino allenylphosphonates.

According to Gomes et *al. J. Org. Chem.*, **2012**, 5439 – 5444.



Diethyl (1-(*N*-(4-methoxybenzyl)methylsulfonamido)propa-1,2-dien-1-yl)phosphonate (SI01)

Prepared according to the general procedures **A** and **B**. Flash Chromatography: EtOAc/PE 20/80 to 100/0; yellow oil, 1.760 g, 49% yield; R_f = 0.37 (EtOAc); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.30 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.13 (d, J = 10.4 Hz, 2H), 4.64 (s, 2H), 4.20 – 4.00 (m, 4H), 3.79 (s, 3H), 3.00 (s, 3H), 1.36 – 1.27 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 215.9 (d, J = 26.5 Hz), 159.3, 130.4, 127.7, 113.6, 98.1 (d, J = 228.4 Hz), 81.6 (d, J = 11.7 Hz), 63.1 (d, J = 6.2 Hz), 55.1, 52.6, 40.5, 16.1 (d, J = 6.6 Hz); ^{31}P NMR (101.25 MHz, $CDCl_3$) δ 10.1; HRMS (ESI) m/z [MH^+] calcd for $C_{16}H_{25}NO_6PS$: 390.1135, found: 390.1135.



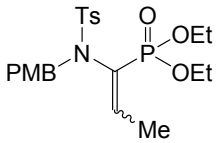
Dimethyl (1-((*N*-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)-3-methylbuta-1,2-dien-1-yl)phosphonate (SI02)

Prepared according to the general procedures **A** and **B**. Flash Chromatography: EtOAc/PE 20/80 to 100/0; yellow solid, 2.146 g, 65% yield; R_f = 0.15 (EtOAc/PE = 60/40); mp = 105-110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 6.81 (d, J = 8.6 Hz, 2H), 4.51 (s, 2H), 3.77 (s, 3H), 3.55 (d, J = 11.1 Hz, 6H), 2.43 (s, 3H), 1.57 (d, J = 4.6 Hz, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 210.8 (d, J = 25.8 Hz), 159.1, 143.4, 136.5, 130.2, 129.4, 127.9, 113.6, 105.0 (d, J = 12.2 Hz), 94.4 (d, J = 237.5 Hz), 55.2, 53.0 (d, J = 6.1 Hz), 52.5, 21.5, 19.2 (d, J = 4.8 Hz); ^{31}P NMR (101.25 MHz, $CDCl_3$) δ 14.6; HRMS (ESI) m/z [MH^+] calcd for $C_{22}H_{29}NO_6PS$: 466.1448, found: 466.1447.

GENERAL PROCEDURE C FOR THE REDUCTION OF α-AAPS INTO α-AVPS

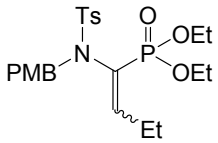
Quinoline (1.5 mmol) and palladium on charcoal (10wt.%; 100 mg) were added to a solution of α-AAP (1.5 mmol) in absolute ethanol (15 mL). The mixture was degassed with hydrogen, and then it was left under a hydrogen atmosphere (balloon) at room temperature for the specified reaction time (20 min to 18 h). After this time, the mixture was filtered through a pad of Celite®, and the solvent was removed from the filtrate in vacuo. The crude product was purified by flash chromatography on silica gel to give the α-AVP.

According to Adler et *al. Eur. J. Org. Chem.* **2013**, 7546–7555.



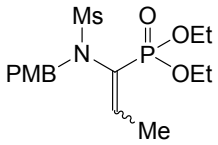
Diethyl (1-((*N*-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)prop-1-en-1-yl)phosphonate (SI03)

Prepared according to the general procedure **C**. Flash Chromatography: EtOAc/PE 10/90 to 90/10; yellow oil, 1.98 g, 50% yield; R_f = 0.55 (EtOAc/PE = 80/20); *Z* stereoisomer: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.23 (m, 2H), 7.21 – 7.12 (m, 2H), 6.79 – 6.72 (m, 2H), 6.20 (dq, *J* = 38.2, 7.5 Hz, 1H), 4.53 (br. s, 2H), 4.13 – 3.83 (m, 4H), 3.77 (s, 3H), 2.41 (s, 3H), 1.90 (dd, *J* = 7.5, 3.1 Hz, 3H), 1.32 – 1.17 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 159.3, 151.8 (d, *J* = 27.1 Hz), 143.4, 137.6, 131.4, 130.8, 129.4, 128.2, 127.7, 126.1, 113.7, 61.9 (d, *J* = 5.8 Hz), 55.3, 53.2, 21.6, 16.4 (d, *J* = 6.3 Hz), 15.3; ^{31}P NMR (101.25 MHz, $CDCl_3$) δ 12.1; Characteristic signals for *E* isomer: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 6.90 – 6.79 (m, 1H), 4.62 (d, *J* = 14.3 Hz, 1H), 4.26 (dd, *J* = 14.3, 1.3 Hz, 1H), 2.42 (s, 3H), 1.45 (dd, *J* = 6.9, 3.0 Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 159.5, 151.2, 113.6, 52.3; ^{31}P NMR (101.25 MHz, $CDCl_3$) δ 13.9; HRMS (ESI) m/z [MNa^+] calcd for $C_{22}H_{30}NNaO_6PS$: 490.1424, found: 490.1411.



Diethyl (1-((*N*-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)but-1-en-1-yl)phosphonate (SI04)

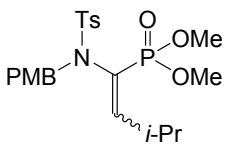
Prepared according to the general procedure **C**. Flash Chromatography: EtOAc/PE 30/70 to 70/30; yellow oil, 331 mg, quantitative yield; R_f = 0.60 (EtOAc/PE = 80/20); IR (neat) 2978, 2932, 2870, 1736, 1613, 1512, 1451 cm^{-1}; *Z* stereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.25 – 7.19 (m, 2H), 7.13 – 7.05 (m, 2H), 6.76 – 6.67 (m, 2H), 5.94 (dt, *J* = 38.2, 8.3 Hz, 1H), 4.46 (br. s, 2H), 4.06 – 3.79 (m, 4H), 3.69 (s, 3H), 2.35 (s, 3H), 2.31 – 2.22 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 6H), 0.77 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.3, 158.1 (d, *J* = 28.0 Hz), 143.4, 137.4, 131.0, 129.4, 128.2, 127.9, 126.2 (d, *J* = 212.0 Hz), 113.6, 61.9 (d, *J* = 5.9 Hz), 55.3, 53.2, 22.6 (d, *J* = 2.7 Hz), 21.6, 16.4 (d, *J* = 6.6 Hz), 12.8 (d, *J* = 1.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 12.3; Characteristic signals for *E* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H), 6.67 – 6.54 (m, 1H), 4.37 (dd, *J* = 138.9, 14.3 Hz, 2H), 2.36 (s, 3H), 0.54 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 157.8 (d, *J* = 26.8 Hz), 137.7, 131.4, 129.4, 128.0, 127.6, 124.8 (d, *J* = 213.7 Hz), 113.6, 62.1 (d, *J* = 6.4 Hz), 52.1, 12.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.2; HRMS (ESI) m/z [MNa^+] calcd for $C_{23}H_{32}NNaO_6PS$: 504.1580, found: 504.1560.



Diethyl (1-(*N*-(4-methoxybenzyl)methylsulfonamido)prop-1-en-1-yl)phosphonate (SI05)

Prepared according to the general procedure **C**. Flash Chromatography: EtOAc/PE 20/80 to 80/20; orange oil, 354 mg, 80% yield; R_f = 0.37 (EtOAc/PE = 90/10); *Z* stereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.22 (dq, *J* = 37.6, 7.6 Hz, 1H), 4.55 (s, 2H), 4.21 – 4.06 (m, 4H), 3.79 (s, 3H), 3.12 (s, 3H), 1.87 (dd, *J* = 7.6, 3.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 153.0 (d, *J* = 28.1 Hz), 130.2, 127.9, 126.3 (d, *J* = 170.0 Hz), 113.5, 61.8 (d, *J* = 5.6 Hz), 54.9, 52.5, 39.6, 16.0 (d, *J* = 6.5 Hz); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 13.3; Characteristic signals for *E* isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.7 Hz, 2H), 6.81 – 6.68 (m, 1H), 4.81 – 4.31 (m, 2H), 3.78 (s, 3H), 3.11 (s, 3H), 1.41 (dd, *J* = 6.9, 3.1 Hz, 3H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 150.8 (d, J = 28.4 Hz), 130.9, 113.3, 62.1 (d, J = 5.8 Hz), 52.0, 39.5, 14.7; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 14.1; HRMS (ESI) m/z [MNa^+] calcd for $C_{16}H_{26}NNaO_6PS$: 414.1111, found: 414.1108.



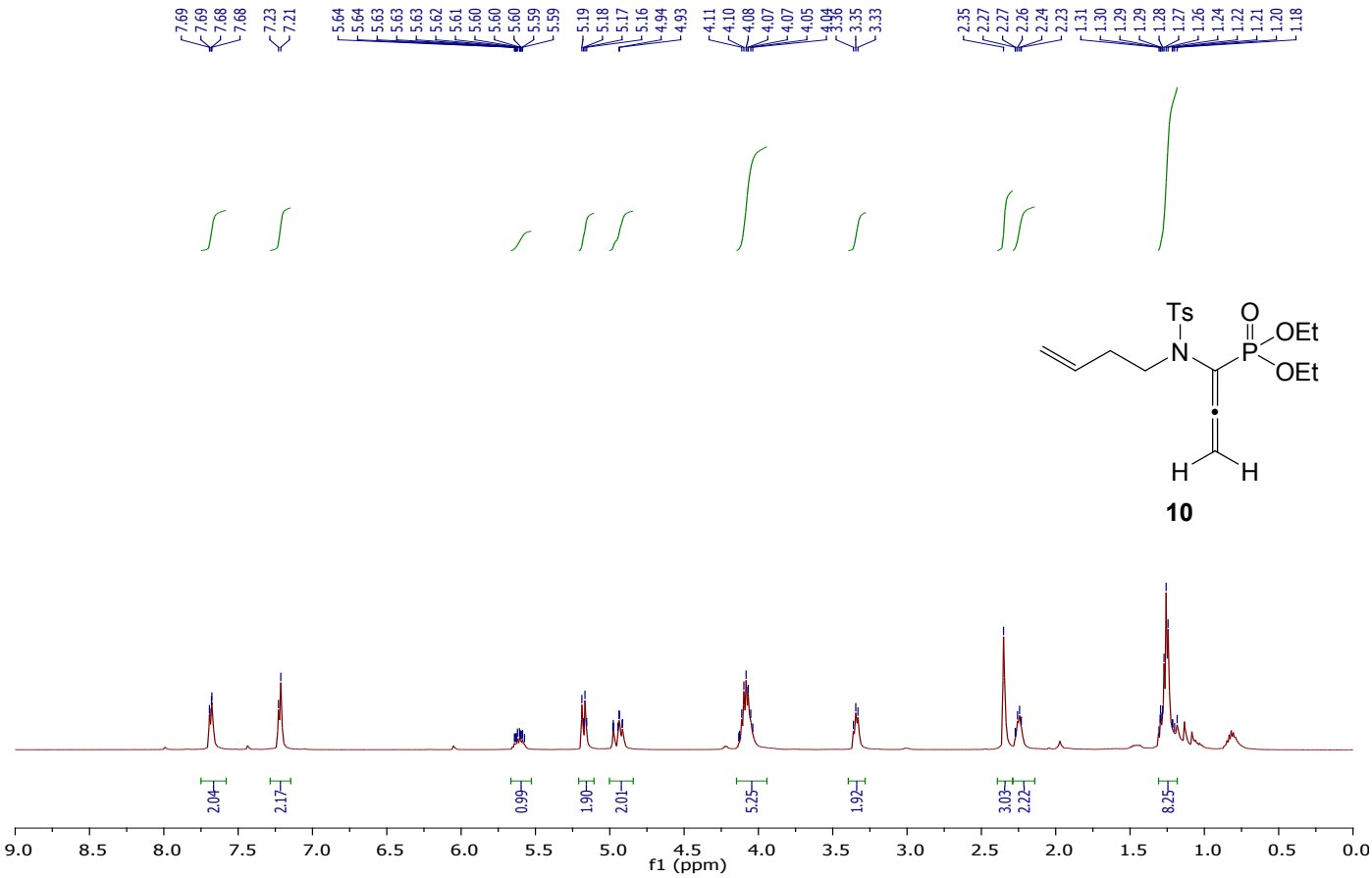
Dimethyl (1-((*N*-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)-3-methylbut-1-en-1-yl)phosphonate (SI06)

Prepared according to the general procedure **C**. Flash Chromatography: EtOAc/PE 70/30; colorless oil, 192 mg, 81% yield; R_f = 0.63 (EtOAc); *Z* stereoisomer ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 5.75 (dd, J = 38.8, 11.4 Hz, 2H), 4.52 (br. s, 1H), 3.78 (s, 3H), 3.62 (d, J = 11.2 Hz, 6H), 3.12 – 2.94 (m, 1H), 2.45 (s, 3H), 0.83 (br. s, 6H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 163.1 (d, J = 28.7 Hz), 159.2, 143.3, 137.0, 131.0, 129.3, 127.9 (d, J = 7.4 Hz), 127.5, 123.6 (d, J = 214.1 Hz), 113.5, 55.2, 53.1, 52.4, 28.3, 21.5 (d, J = 5.5 Hz); ^{31}P NMR (121.25 MHz, $CDCl_3$) δ 15.3; Characteristic signals for *E* isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.3 Hz, 2H), 6.48 (dd, J = 12.8, 10.9 Hz, 1H), 4.67 (d, J = 14.4 Hz, 1H), 4.23 (dd, J = 14.4, 1.6 Hz, 1H), 3.66 (d, J = 11.1 Hz, 6H), 1.05 (d, J = 6.5 Hz, 3H), 0.24 (d, J = 6.5 Hz, 3H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 162.6 (d, J = 25.8 Hz), 159.4, 137.4, 131.2, 123.0, 127.9, 121.5 (d, J = 212.1 Hz), 113.7, 28.8; ^{31}P NMR (121.25 MHz, $CDCl_3$) δ 17.2; HRMS (ESI) m/z [MH^+] calcd for $C_{22}H_{31}NO_6PS$: 468.1579, found: 468.1604.

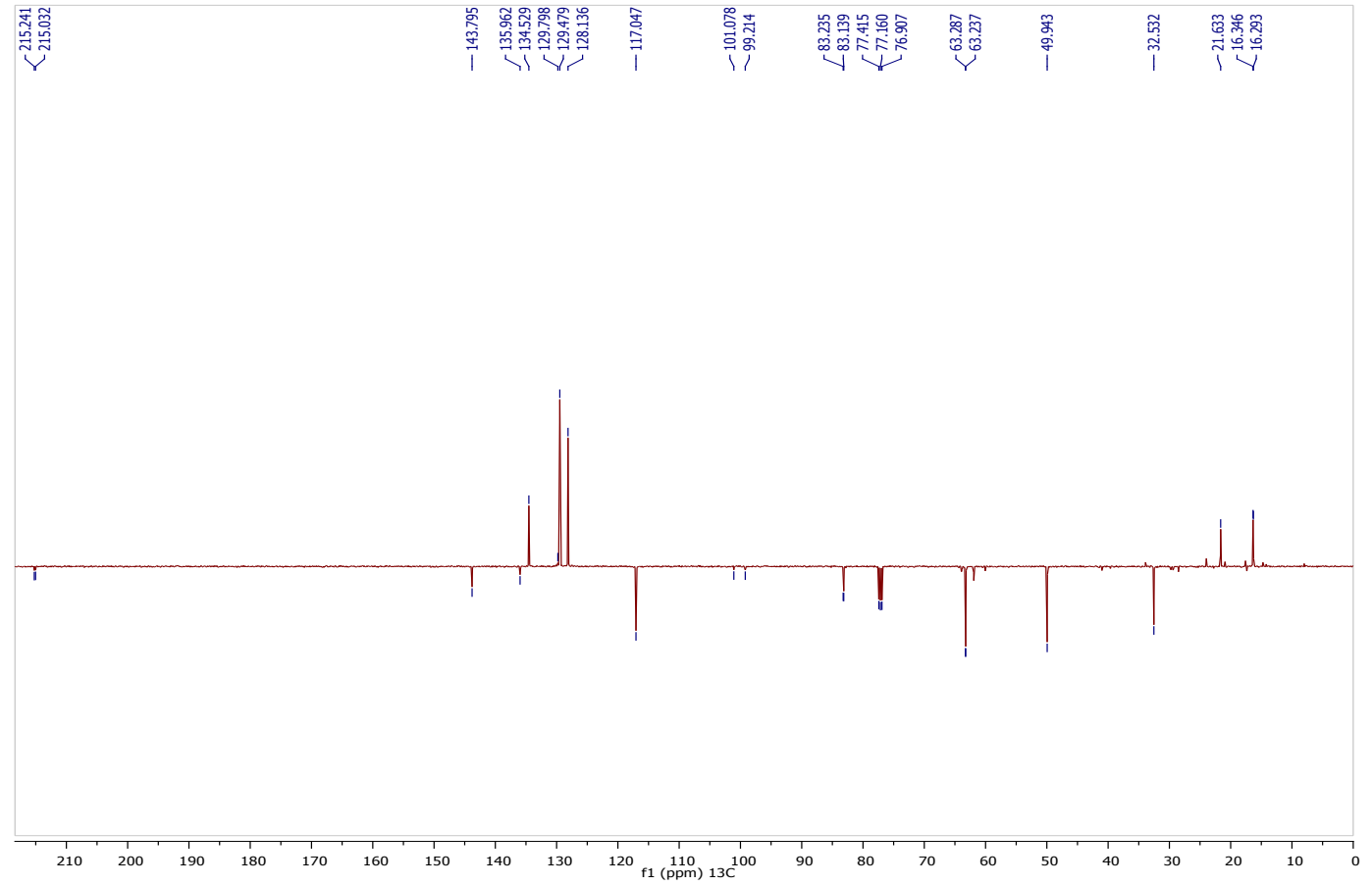
^{1}H AND ^{13}C NMR SPECTRA

SPECTRA OF THE α-AAPS 13

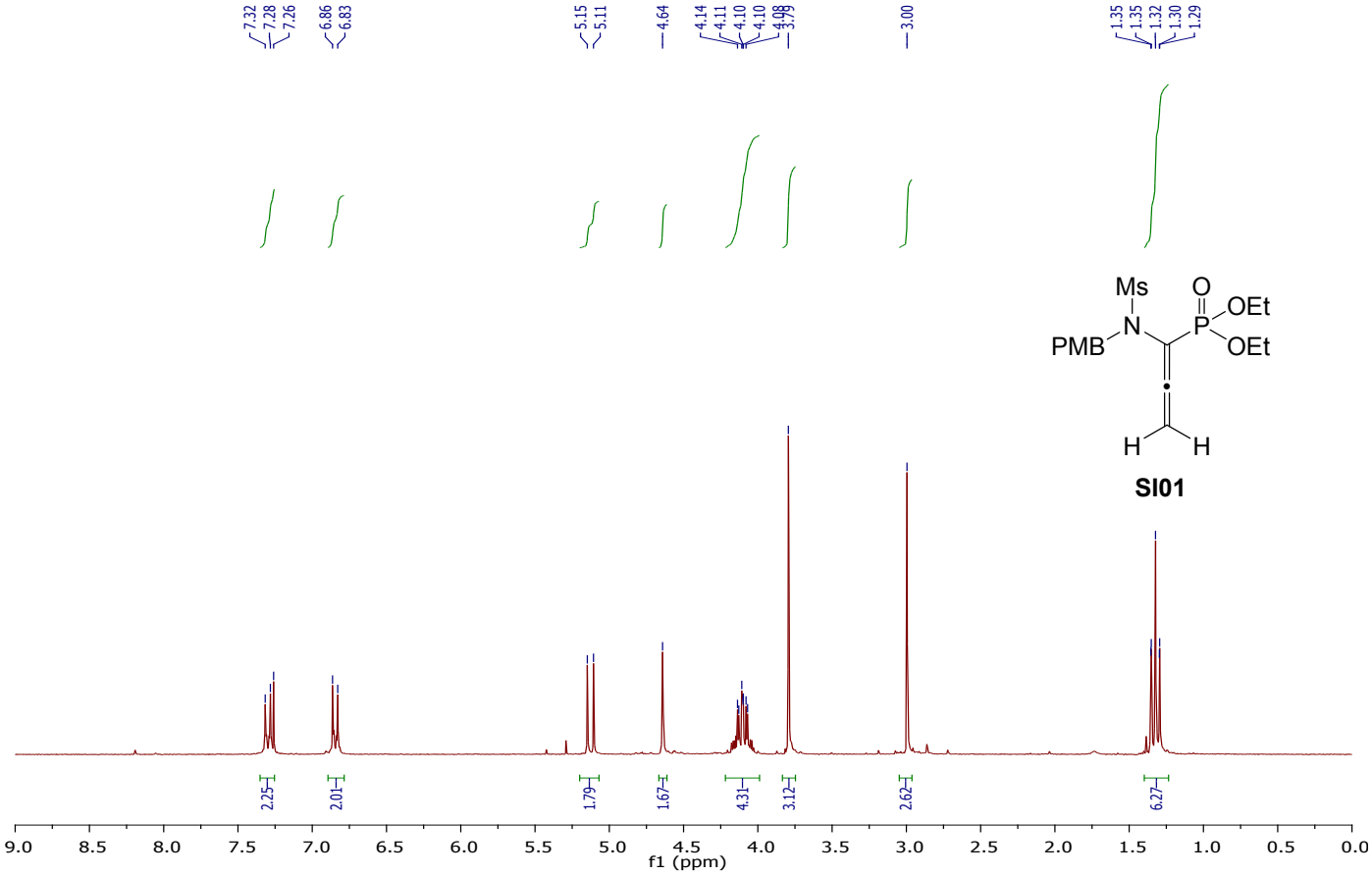
» ^{1}H NMR – 500 MHz – $CDCl_3$



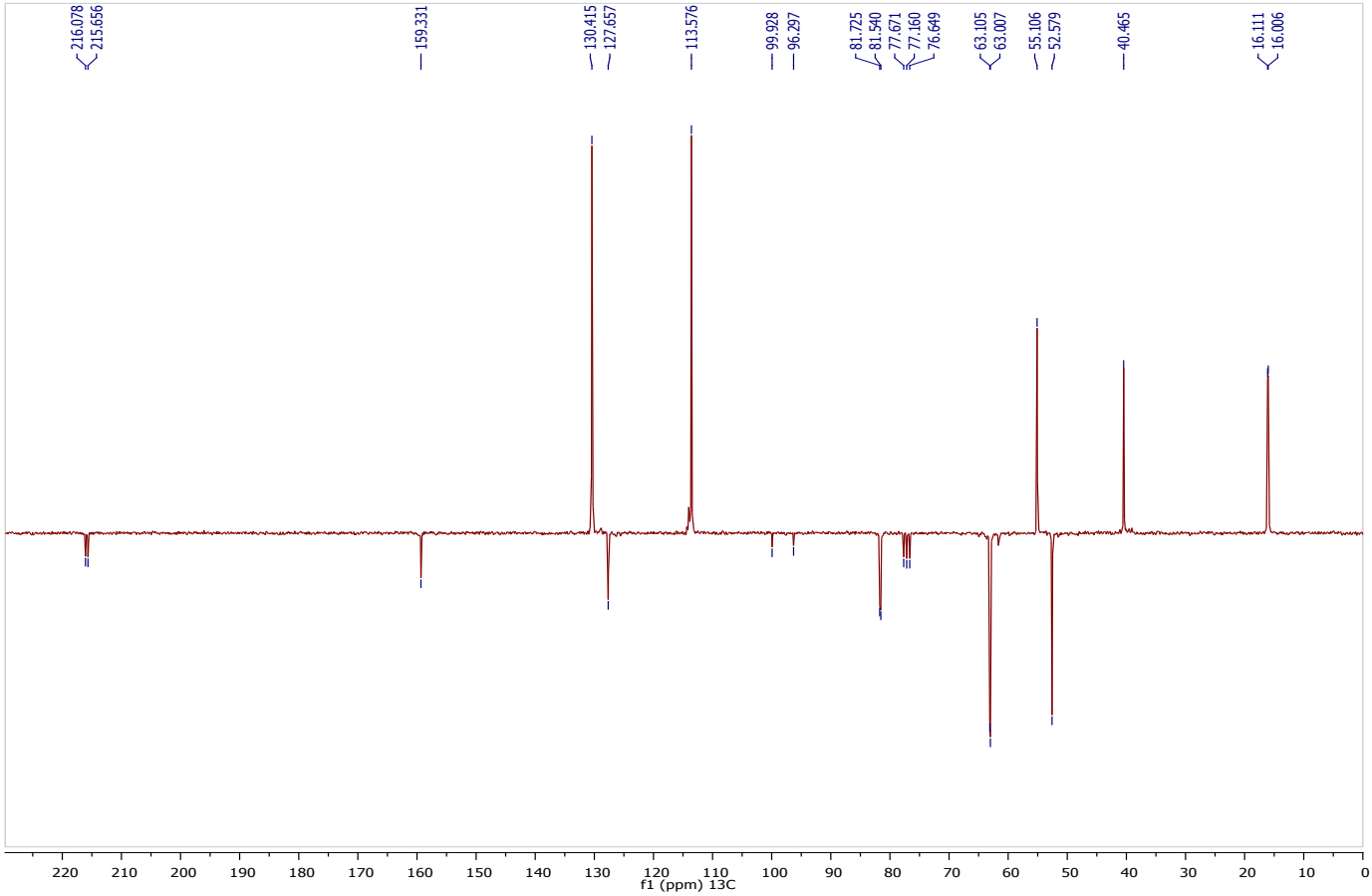
» ^{13}C NMR – 126 MHz – $CDCl_3$



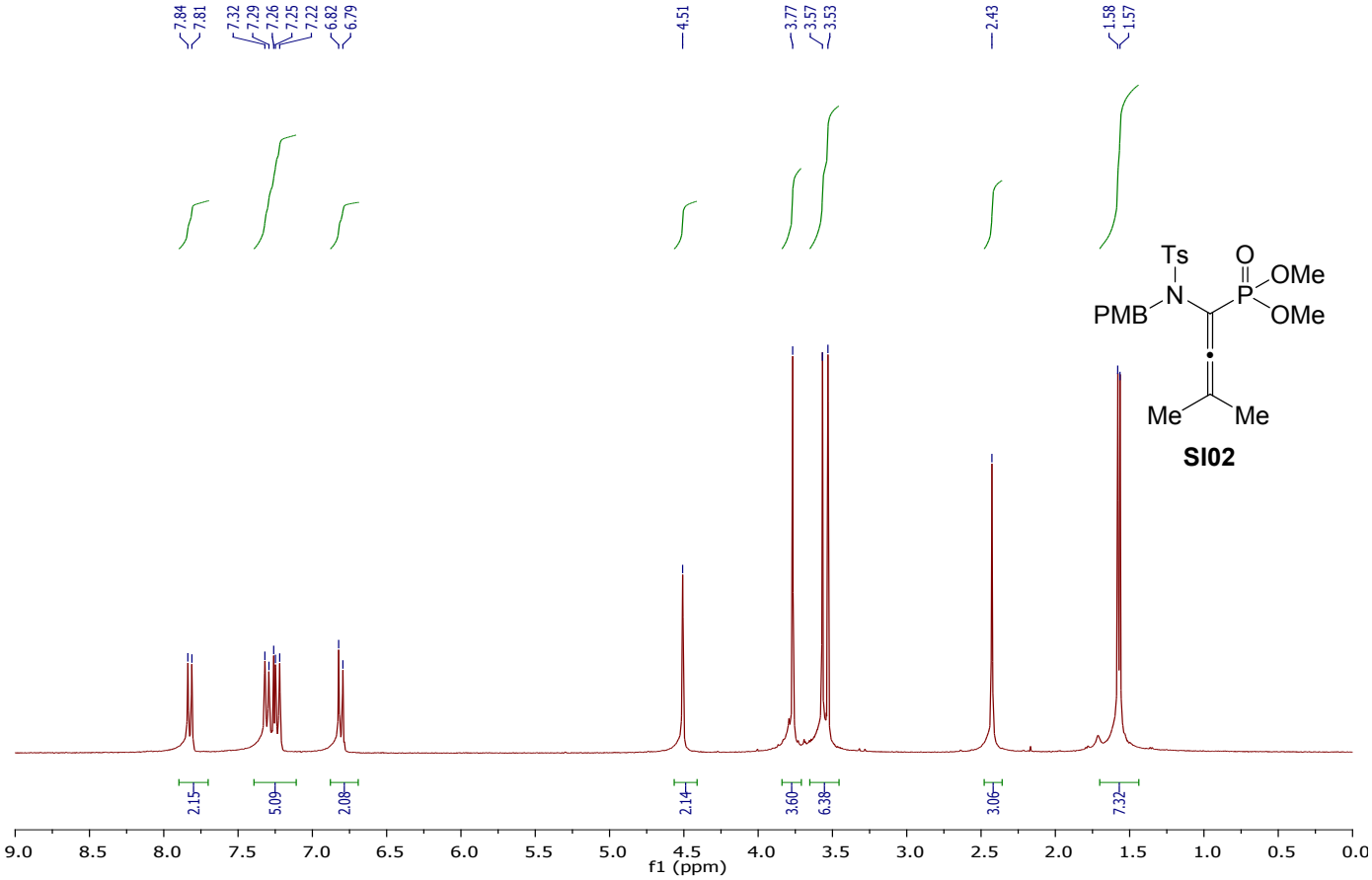
» ^{1}H NMR – 250 MHz – $CDCl_3$



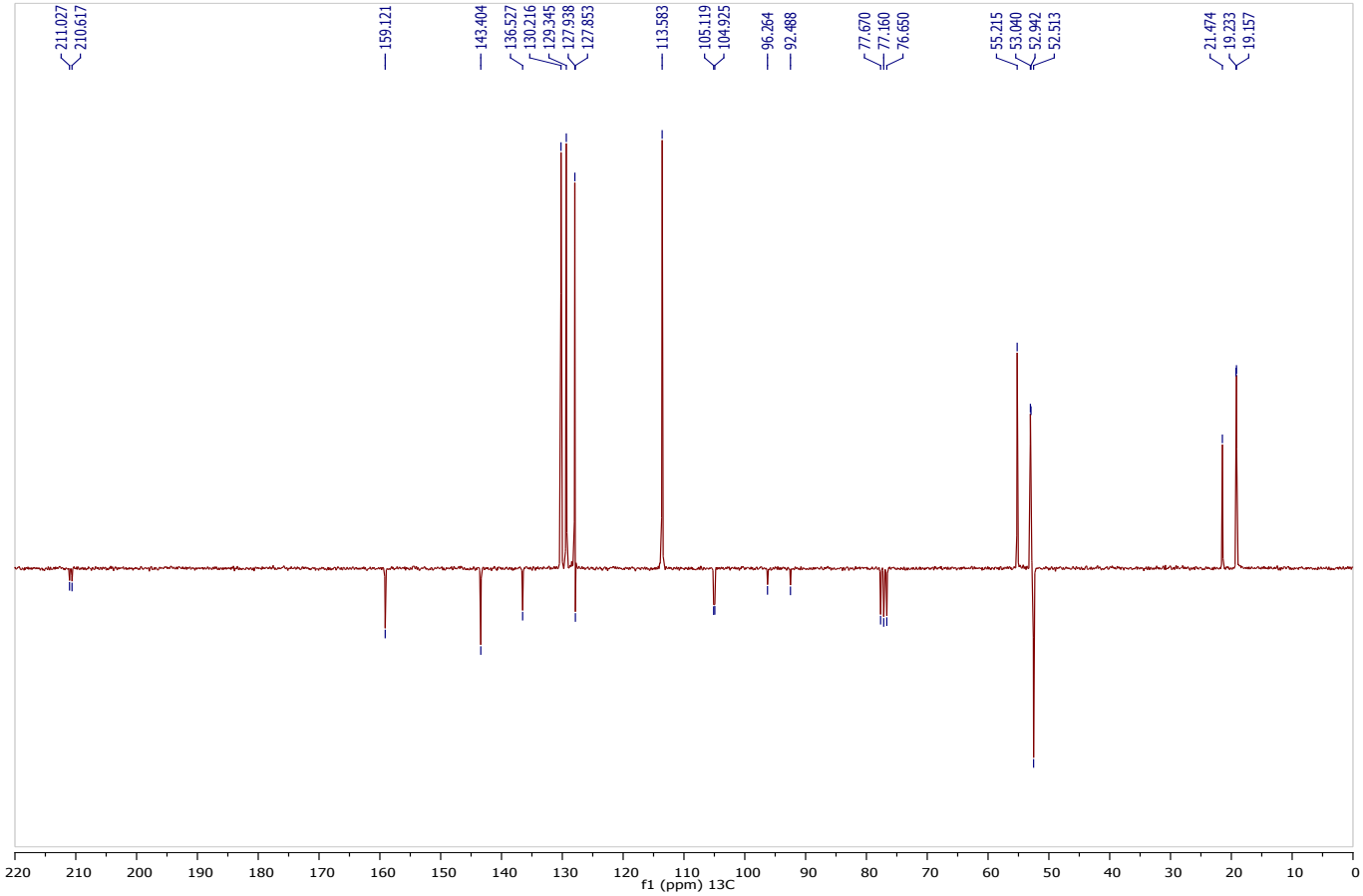
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



» ^{1}H NMR – 250 MHz – $CDCl_3$

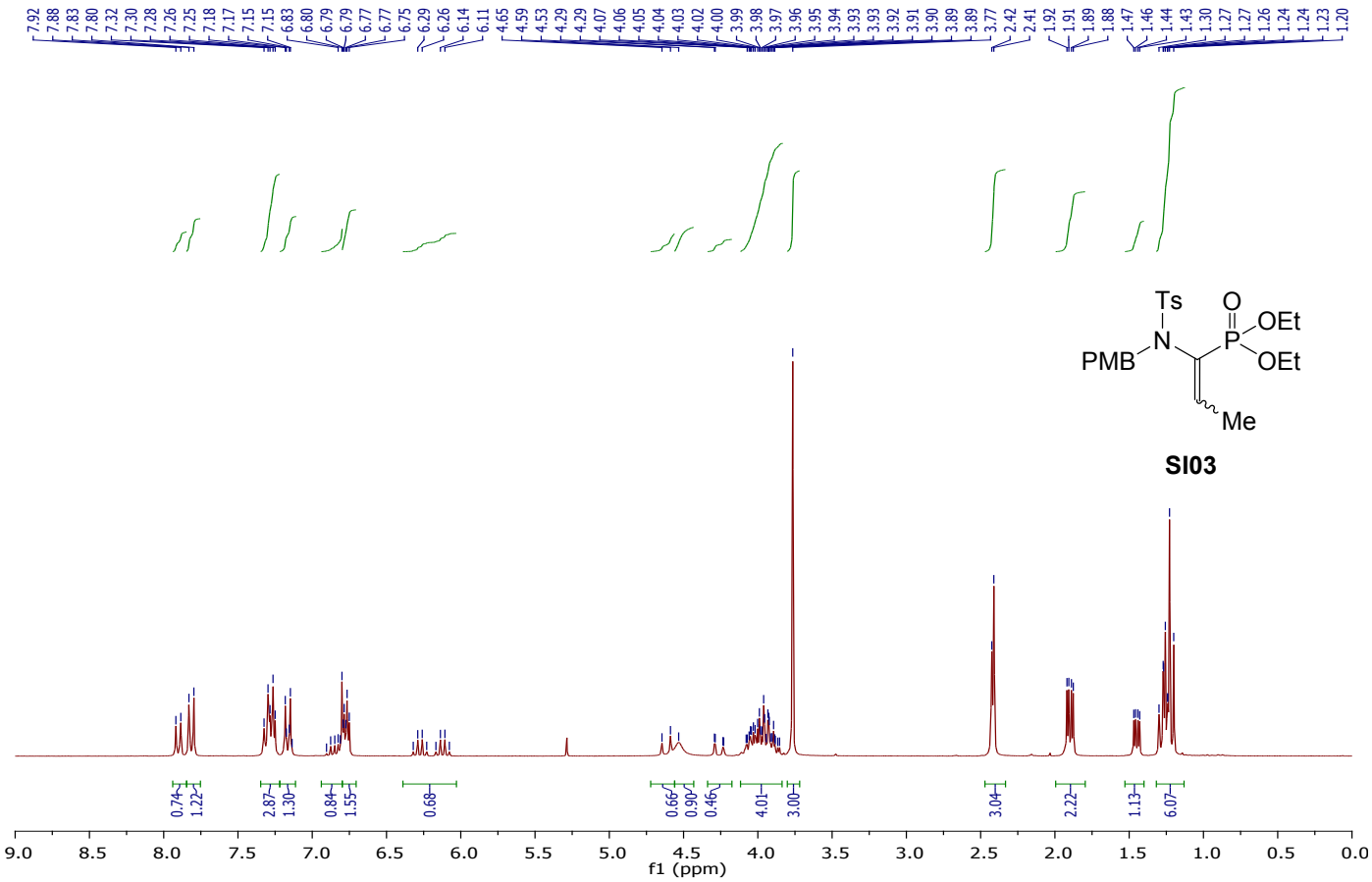


» ^{13}C NMR – 62.9 MHz – $CDCl_3$

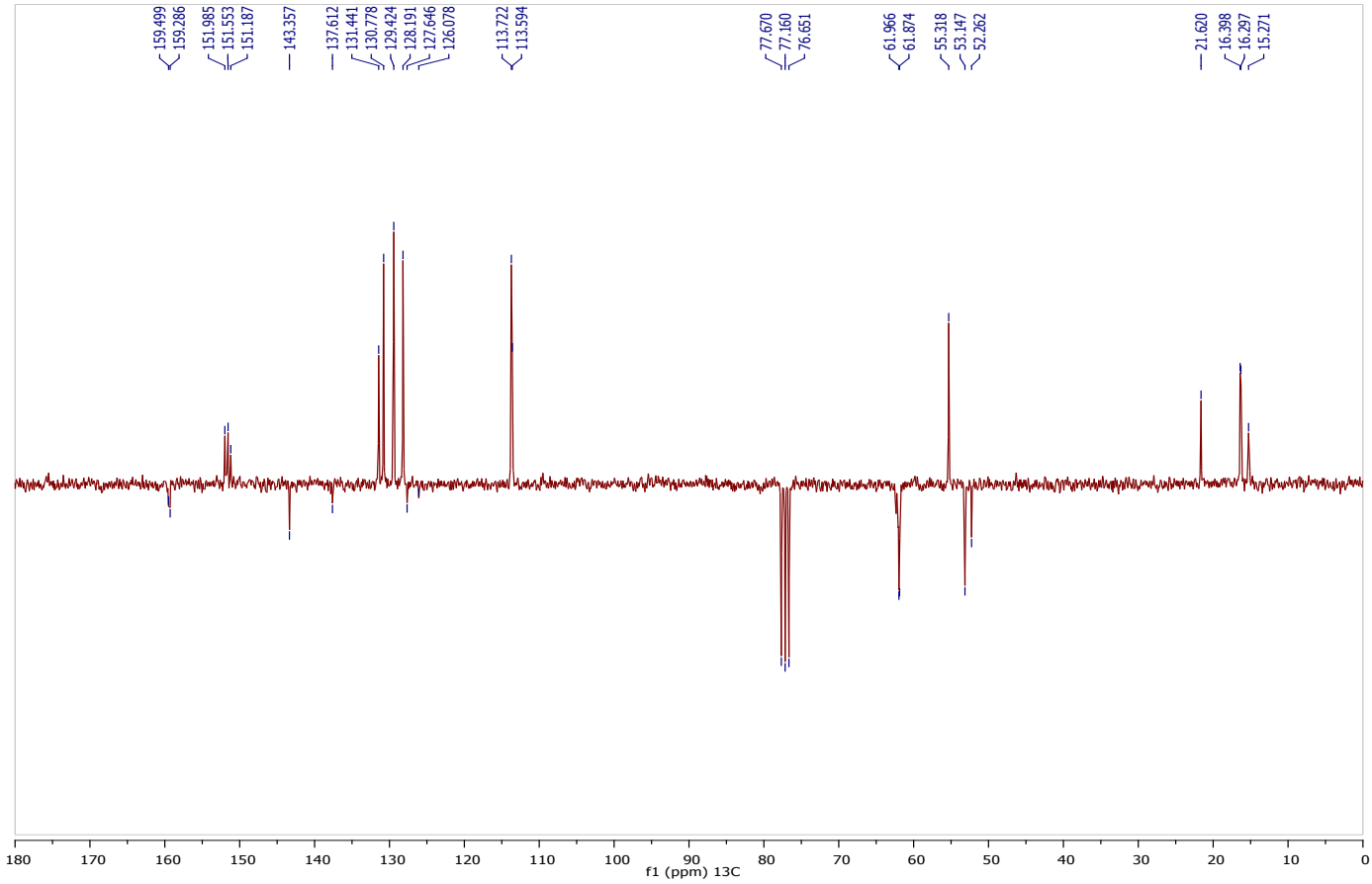


SPECTRA OF THE PMB-PROTECTED α-AVPS 14

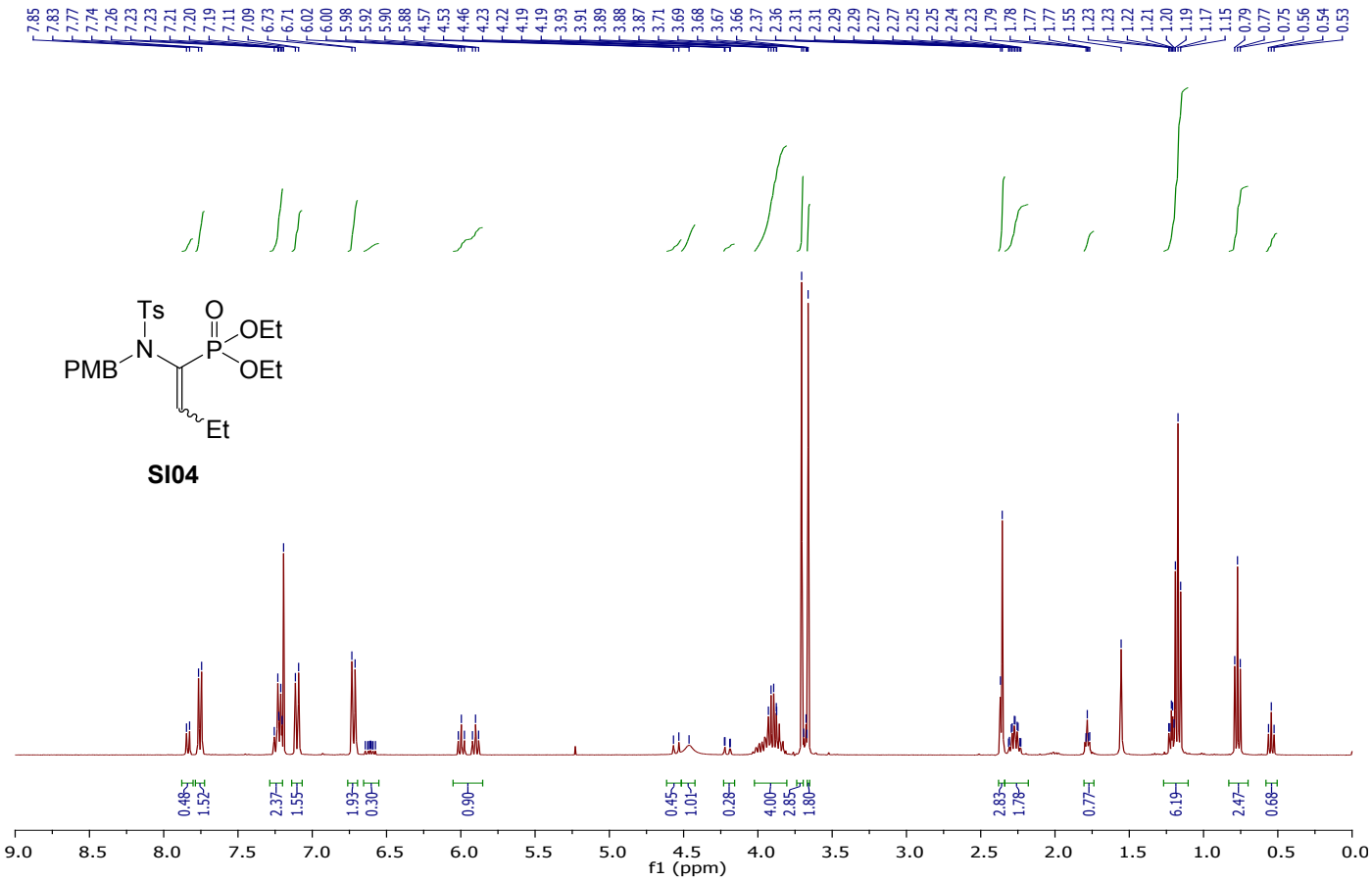
» ^{1}H NMR – 250 MHz – $CDCl_3$



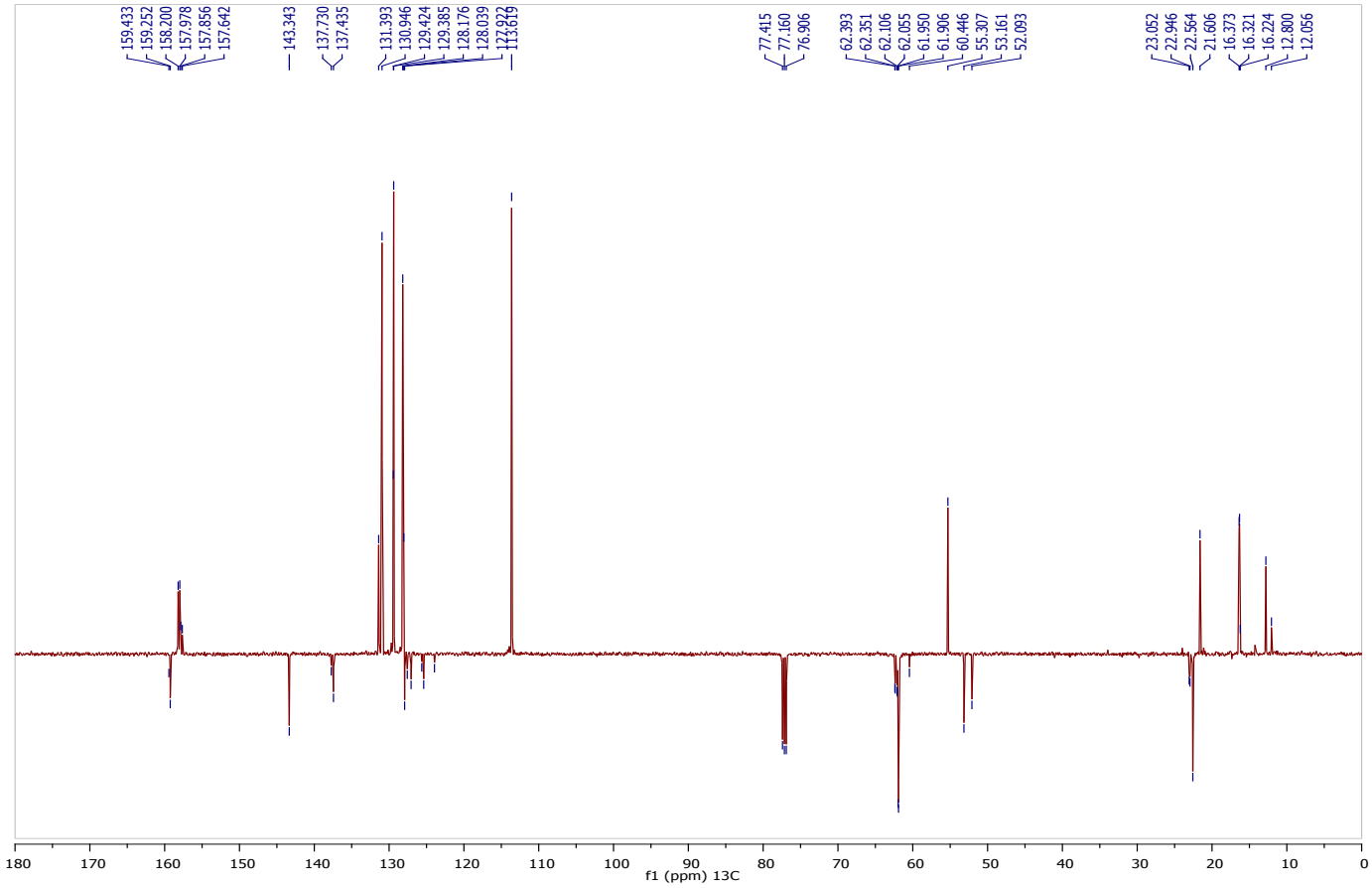
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



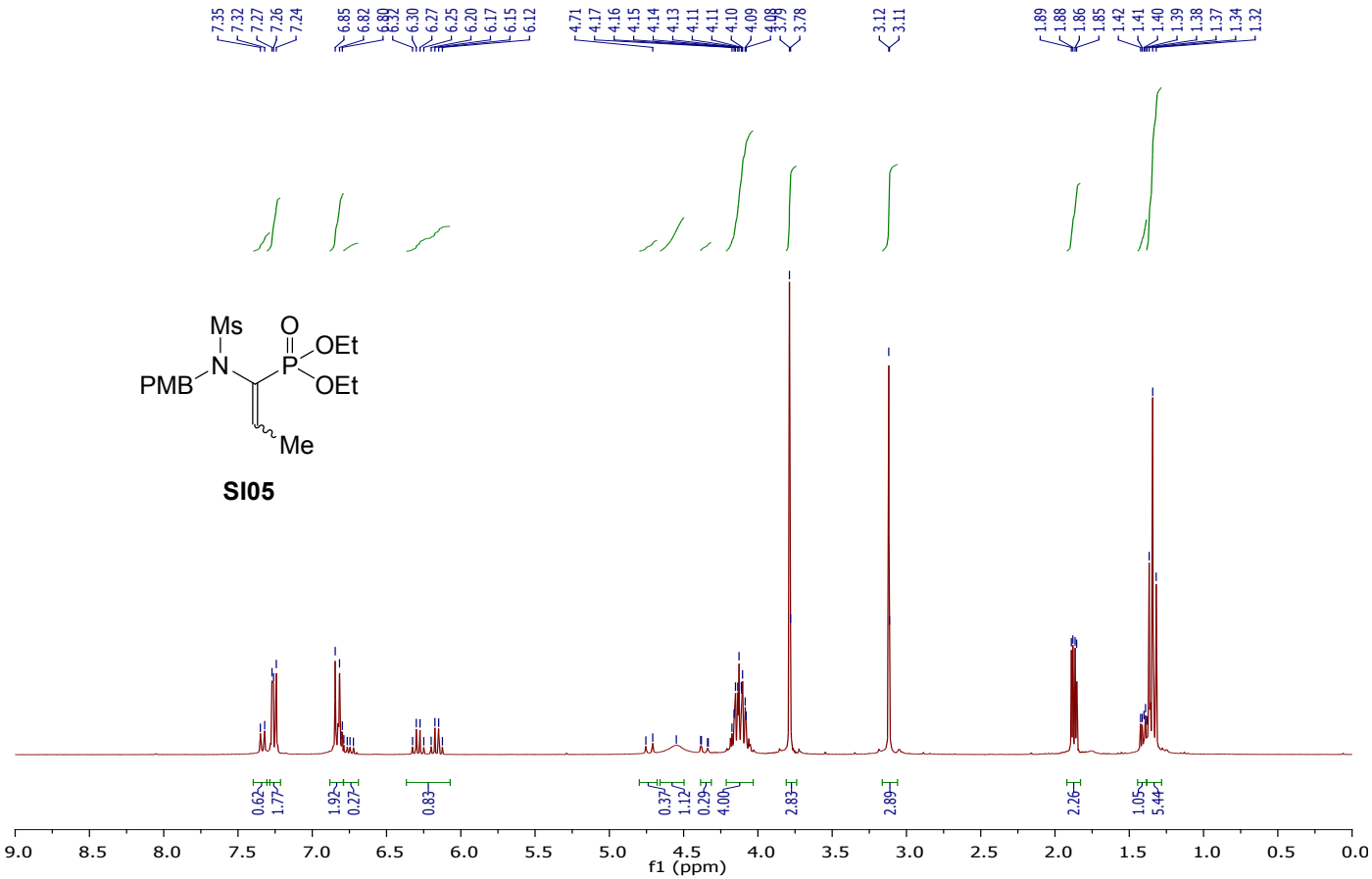
» ^{1}H NMR – 400 MHz – $CDCl_3$



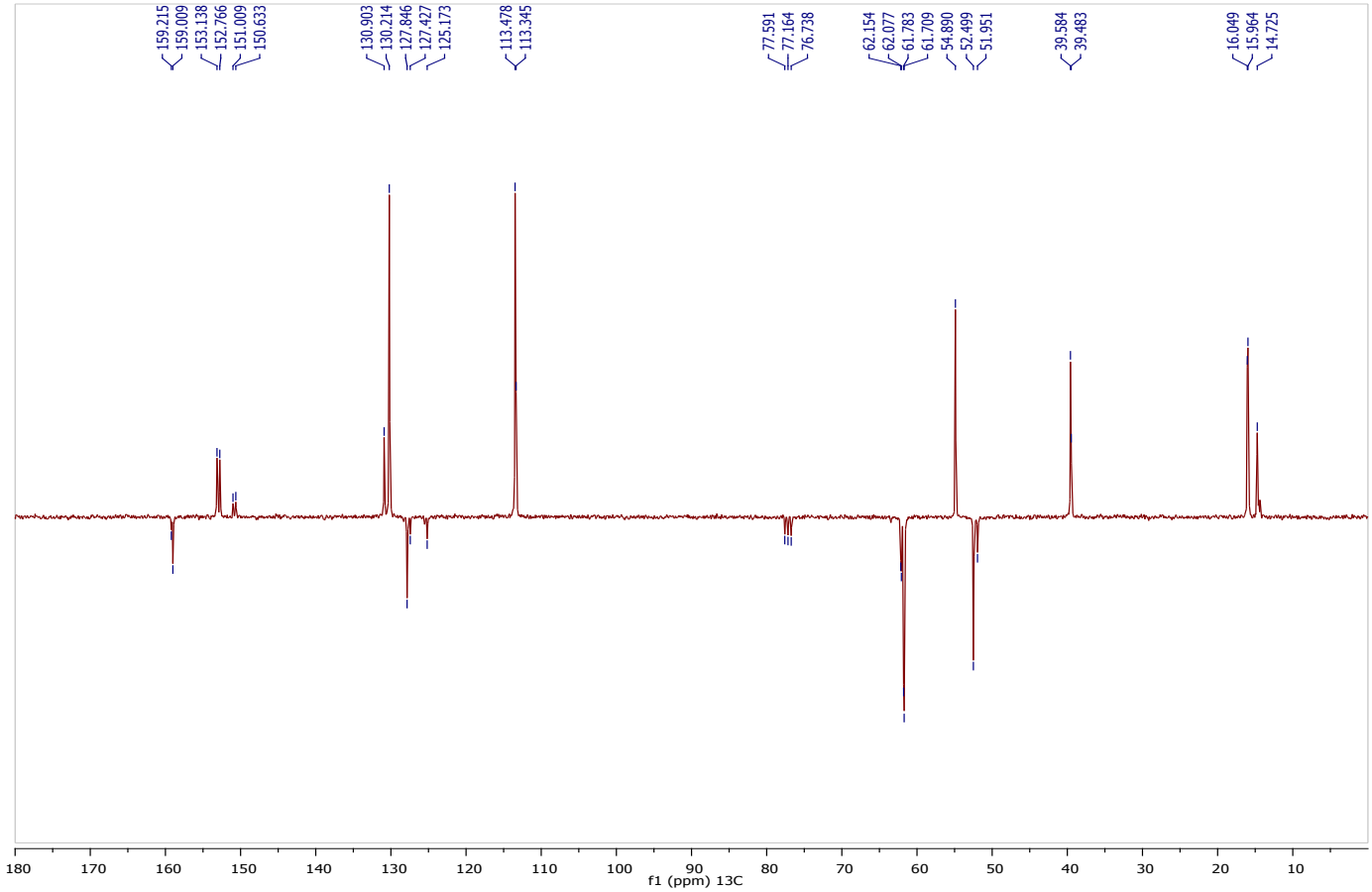
» ^{13}C NMR – 126 MHz – $CDCl_3$



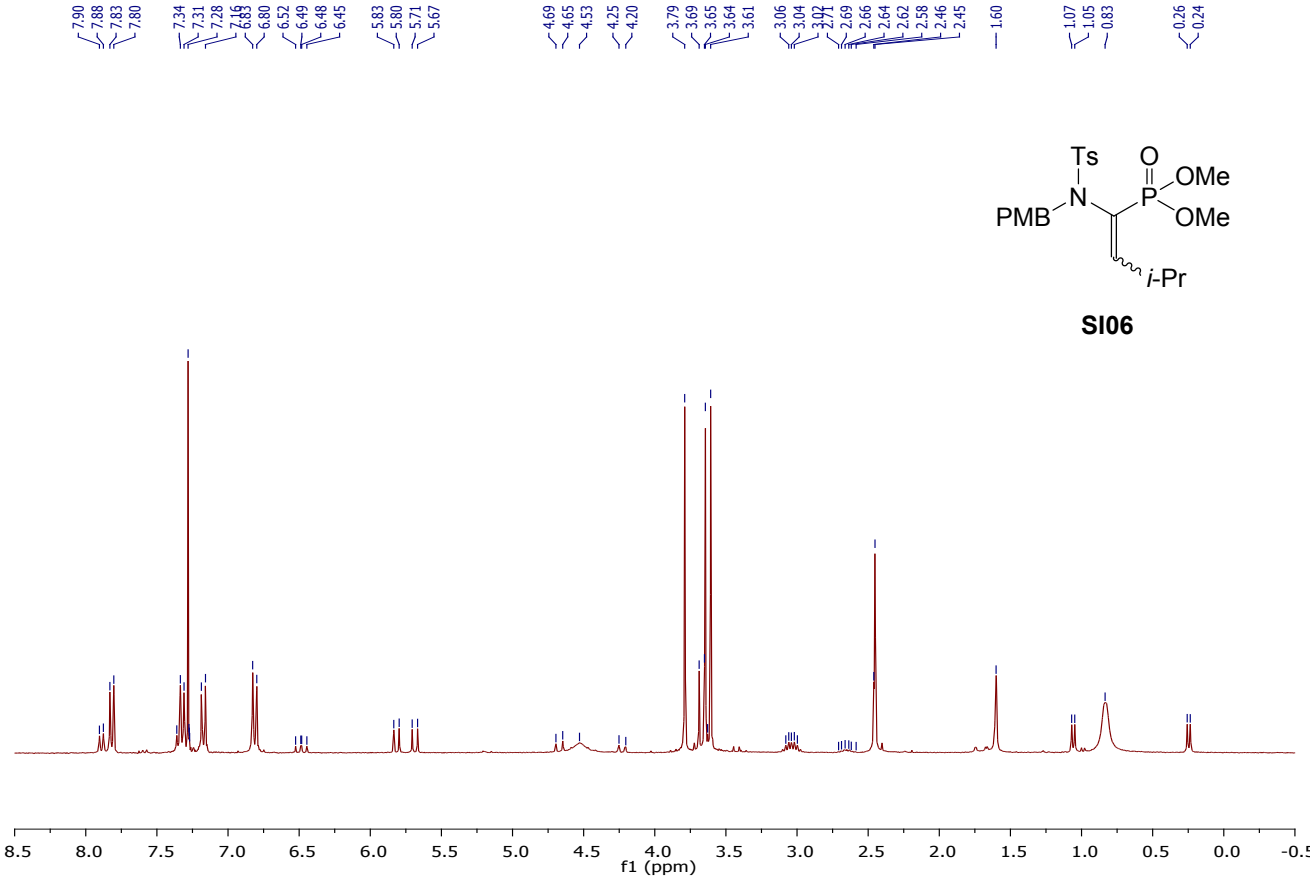
» ^{1}H NMR – 300 MHz – $CDCl_3$



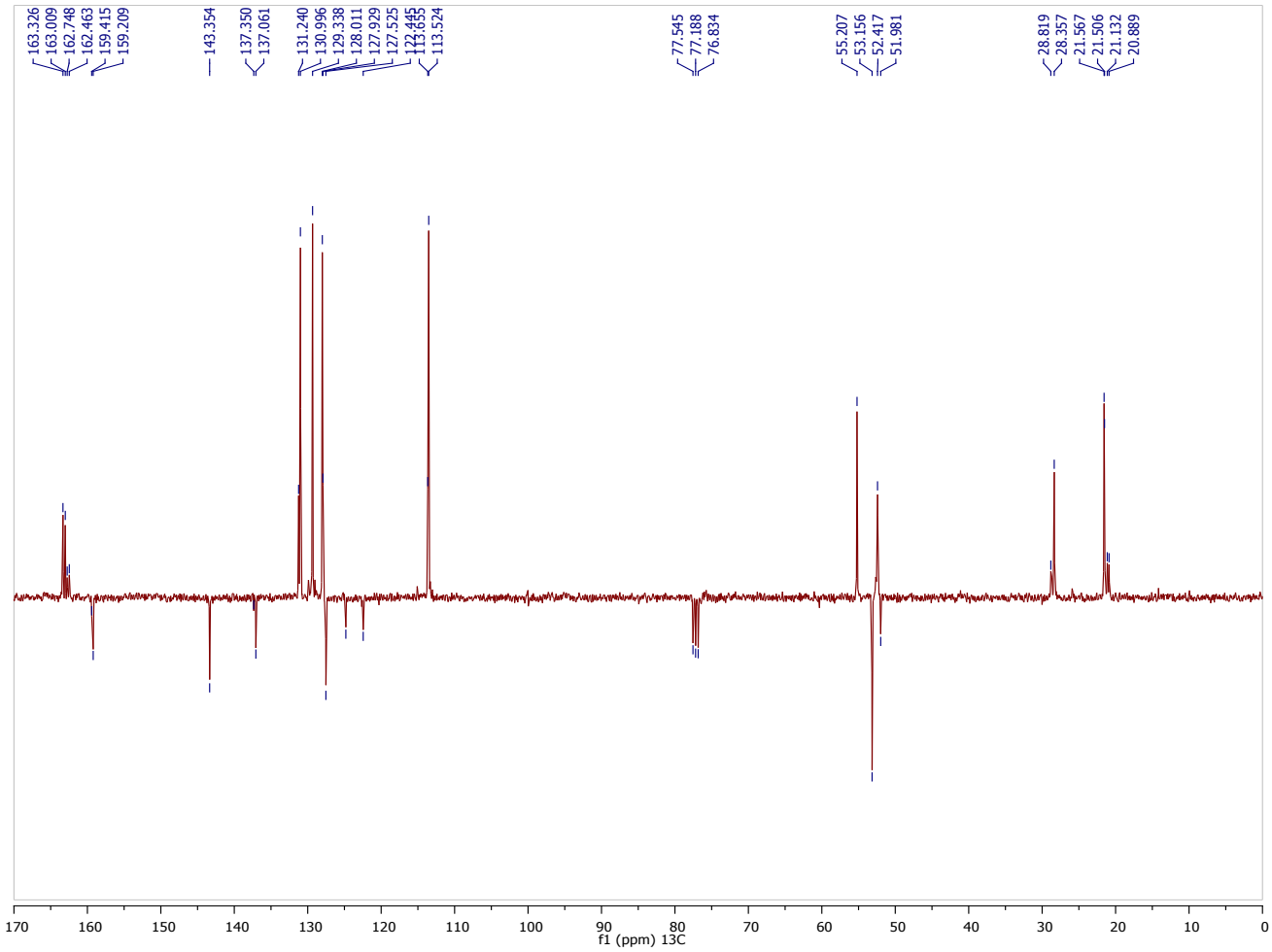
» ^{13}C NMR – 75 MHz – $CDCl_3$



» ^{1}H NMR – 300 MHz – $CDCl_3$

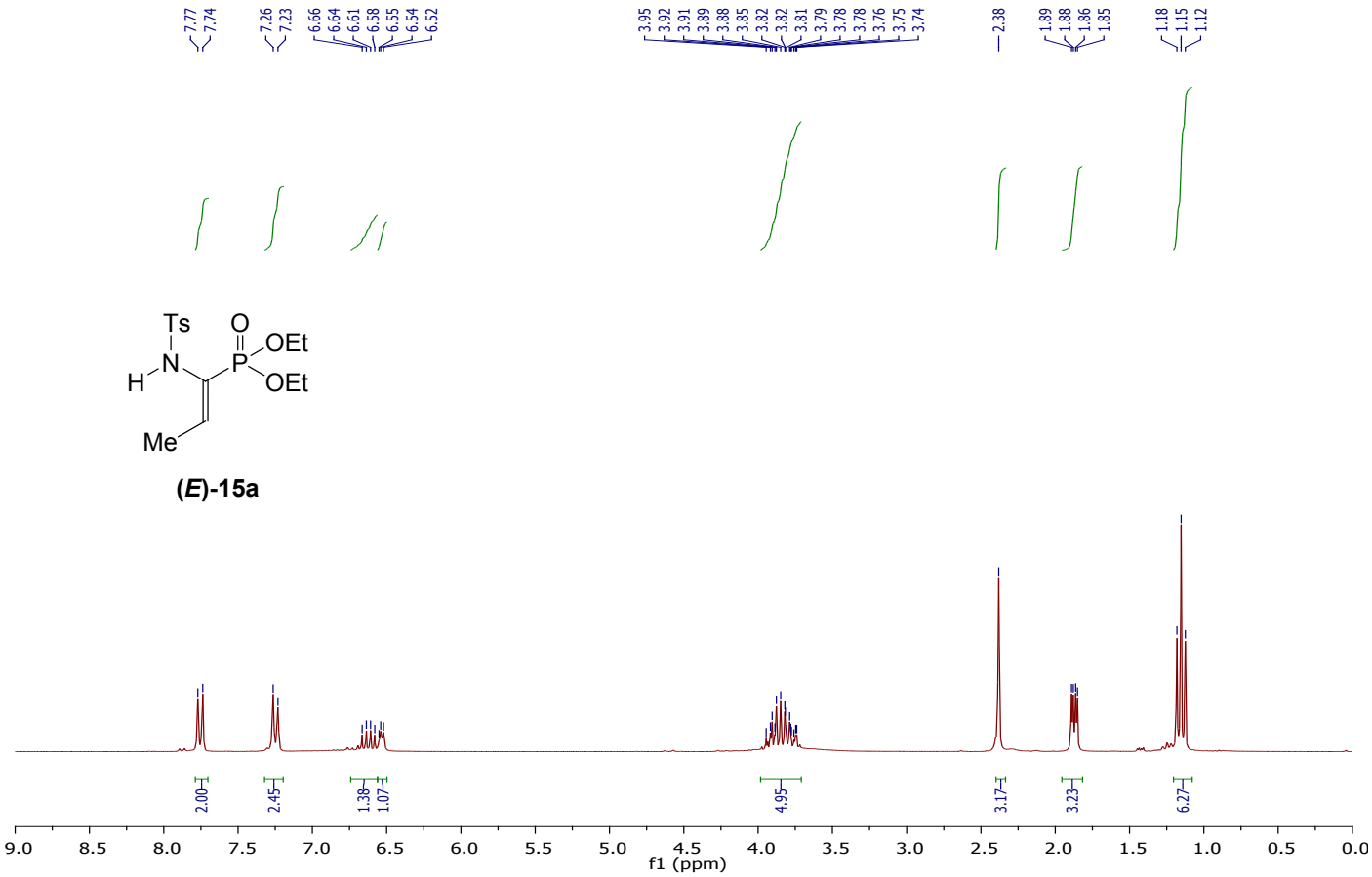


» ^{13}C NMR – 91 MHz – $CDCl_3$

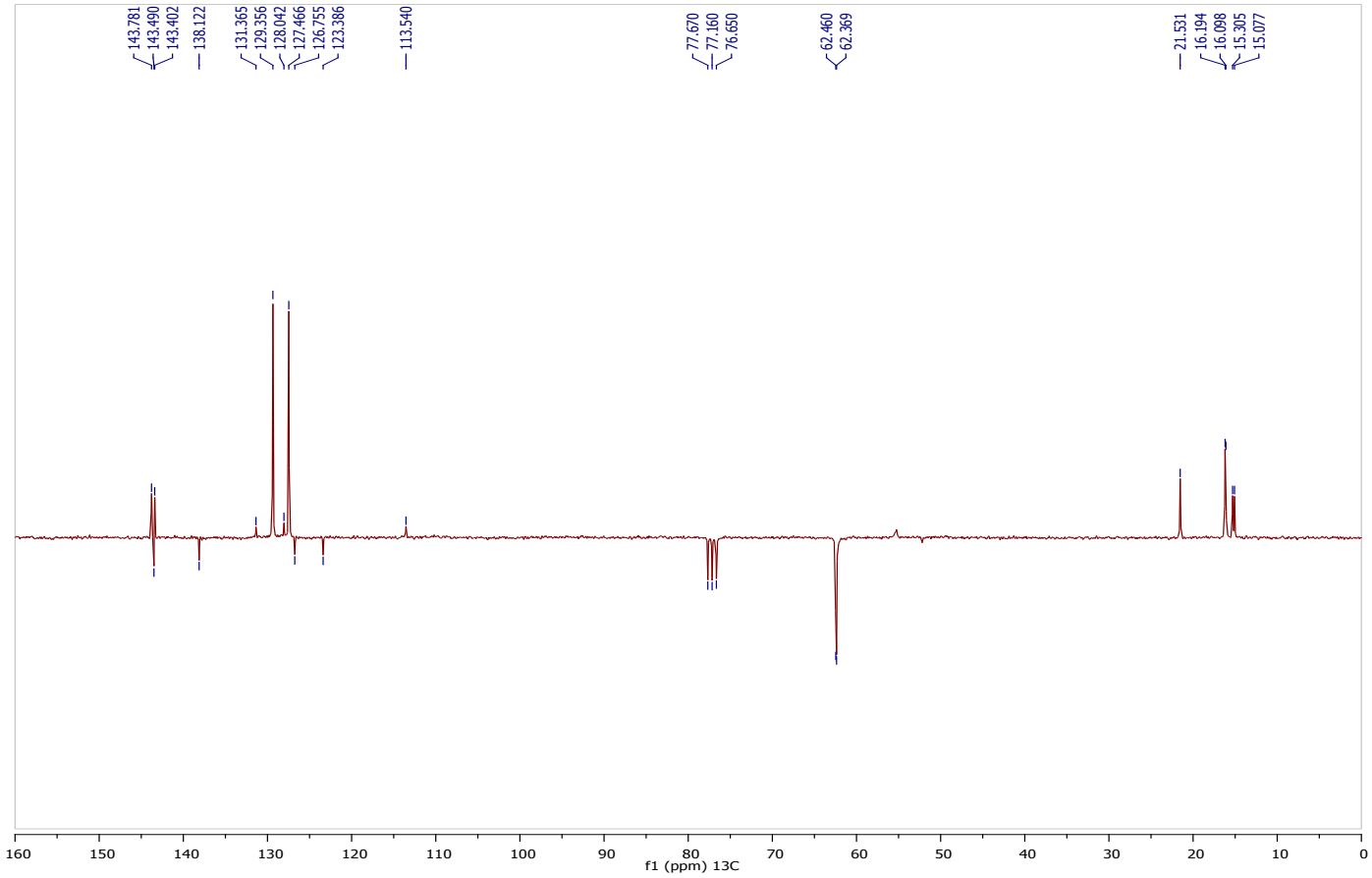


SPECTRA OF THE DEPROTECTED α-AVPS 15

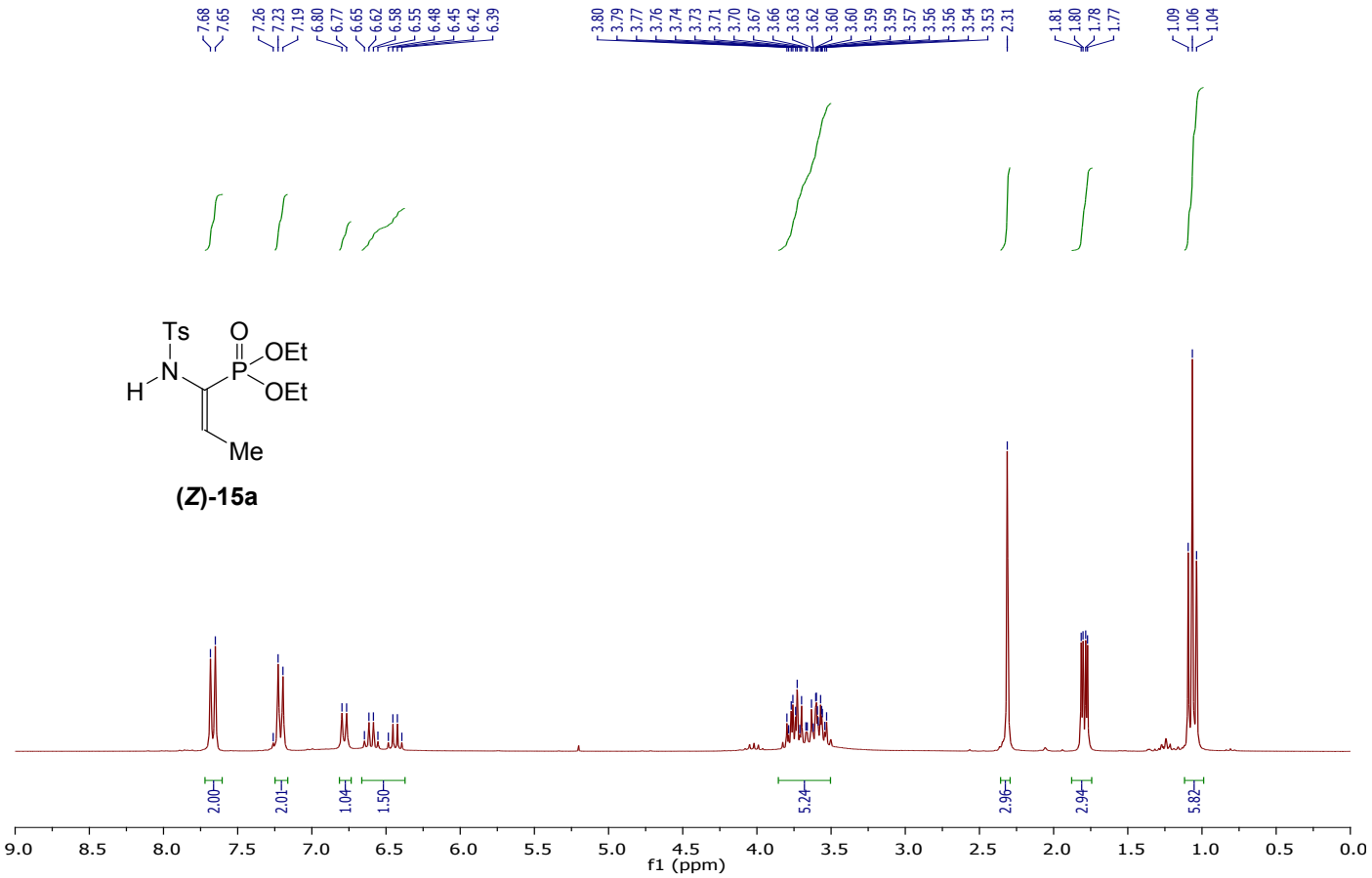
» ^{1}H NMR – 250 MHz – $CDCl_3$



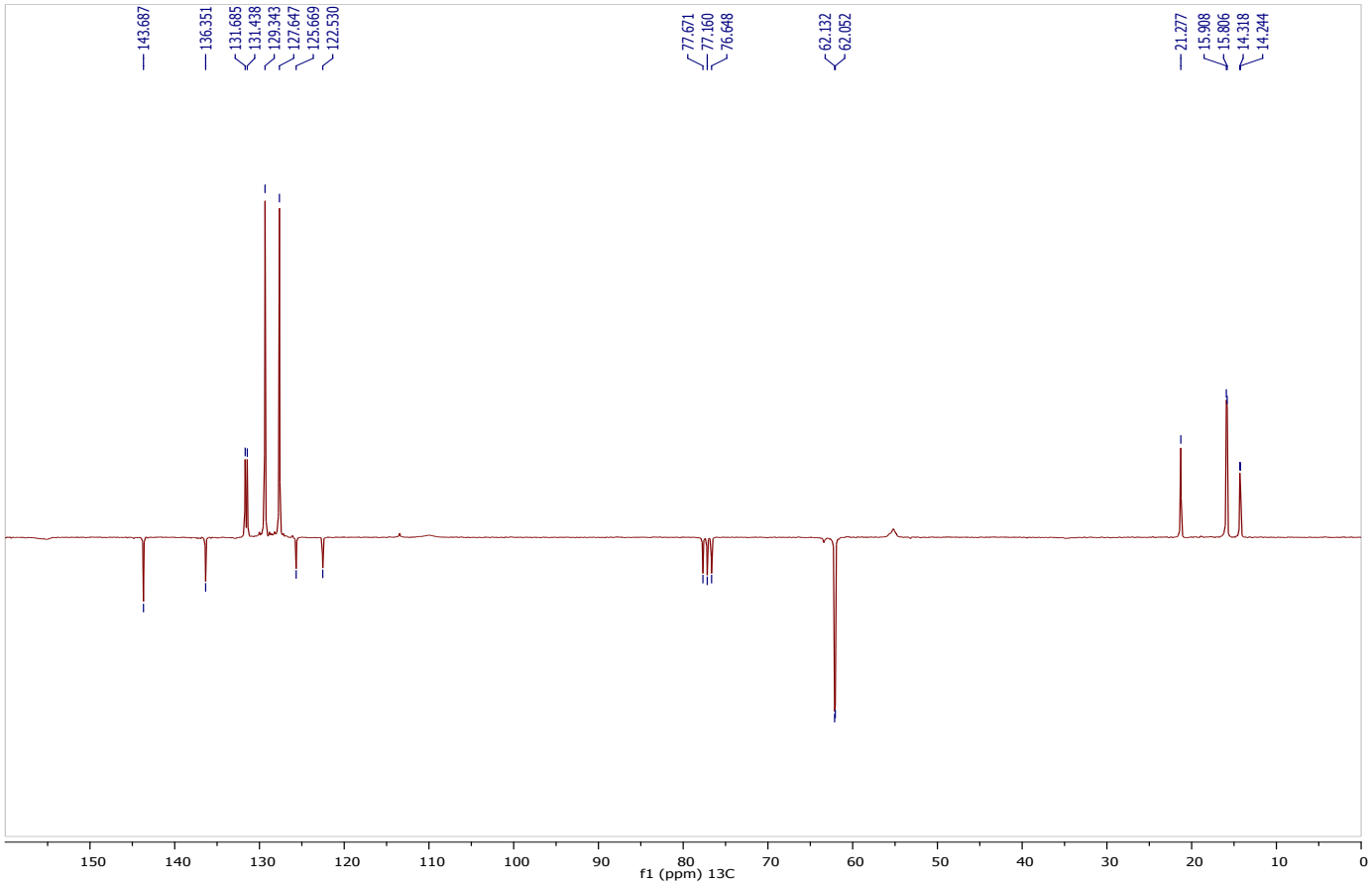
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



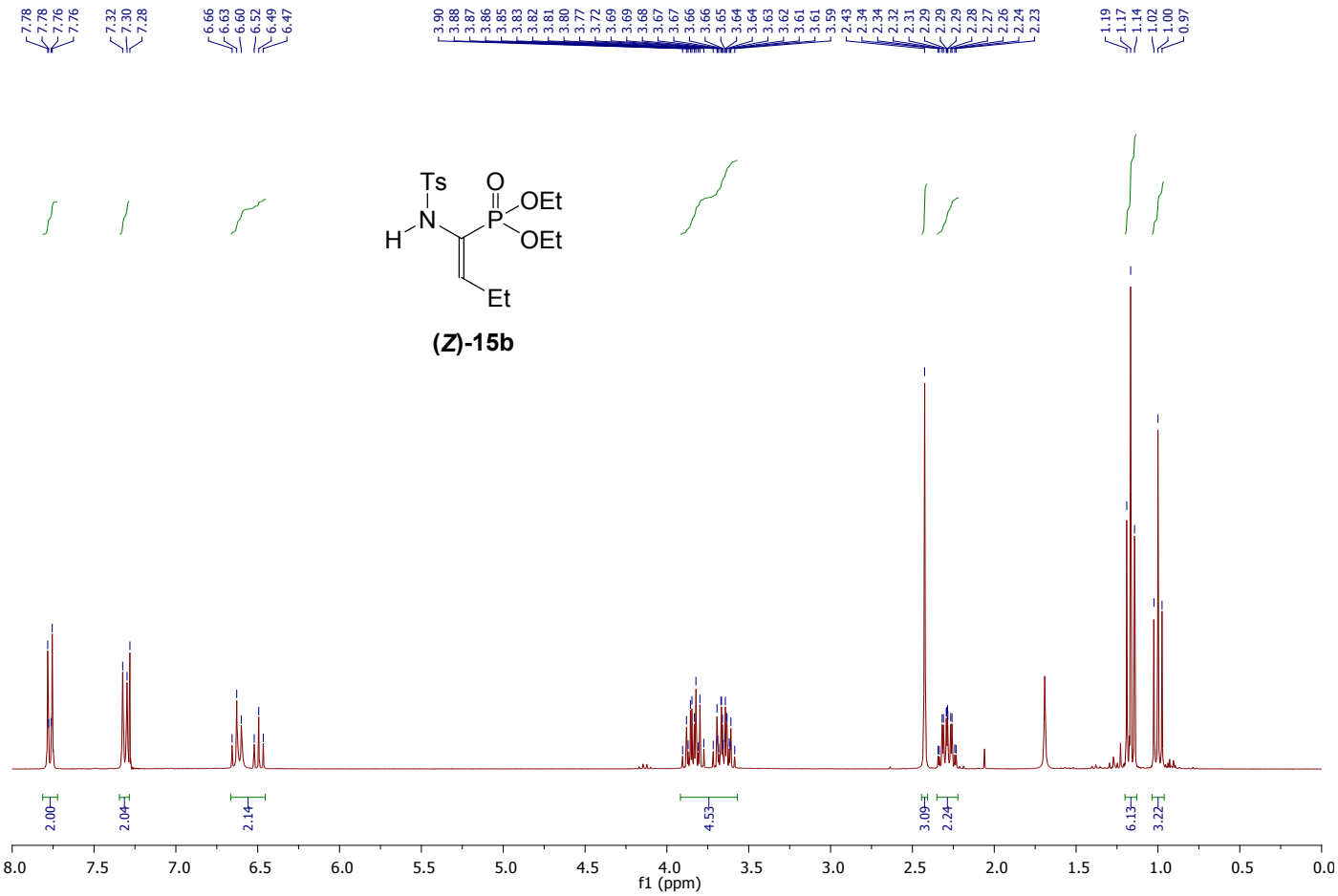
» ^{1}H NMR – 250 MHz – $CDCl_3$



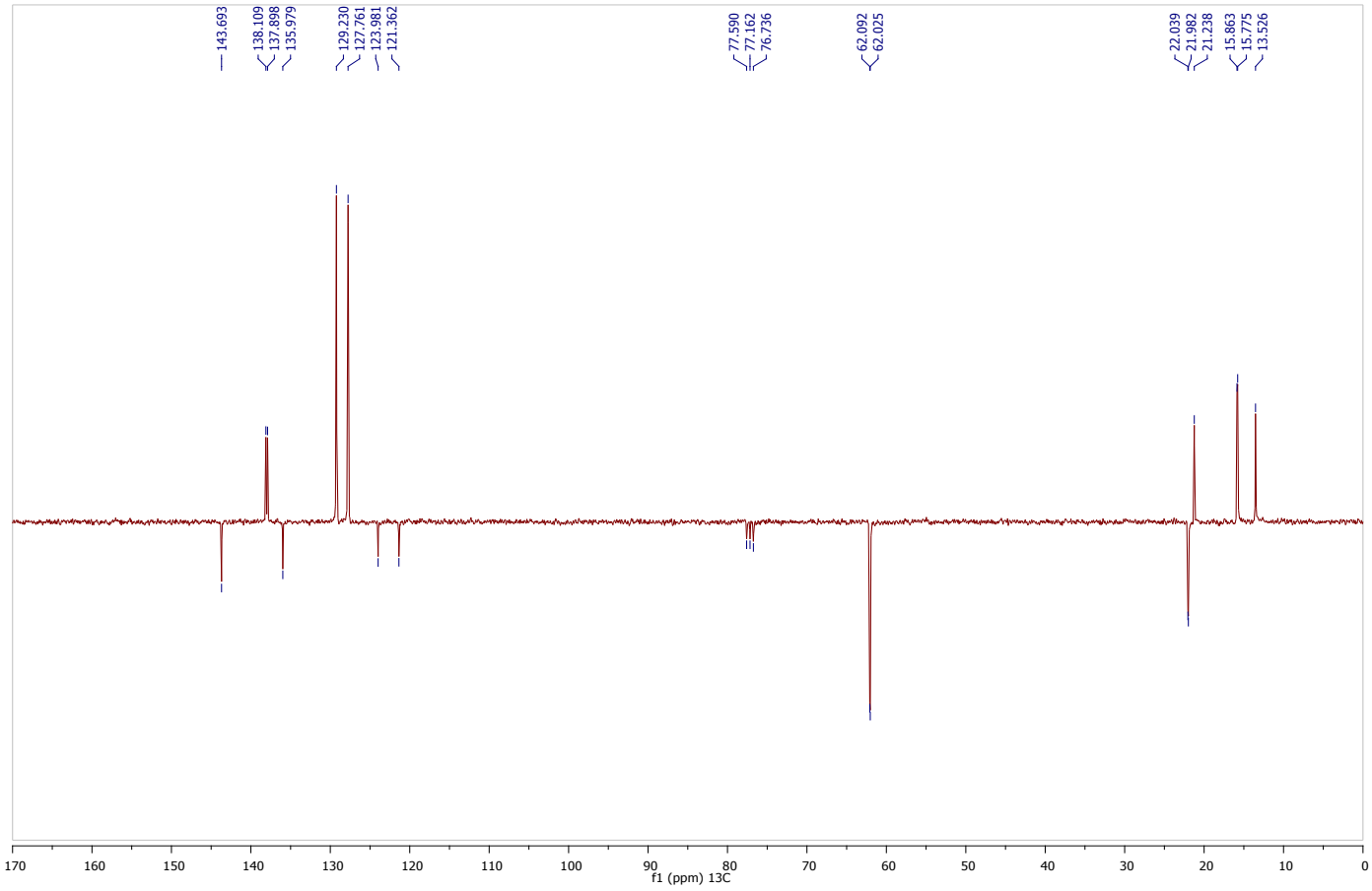
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



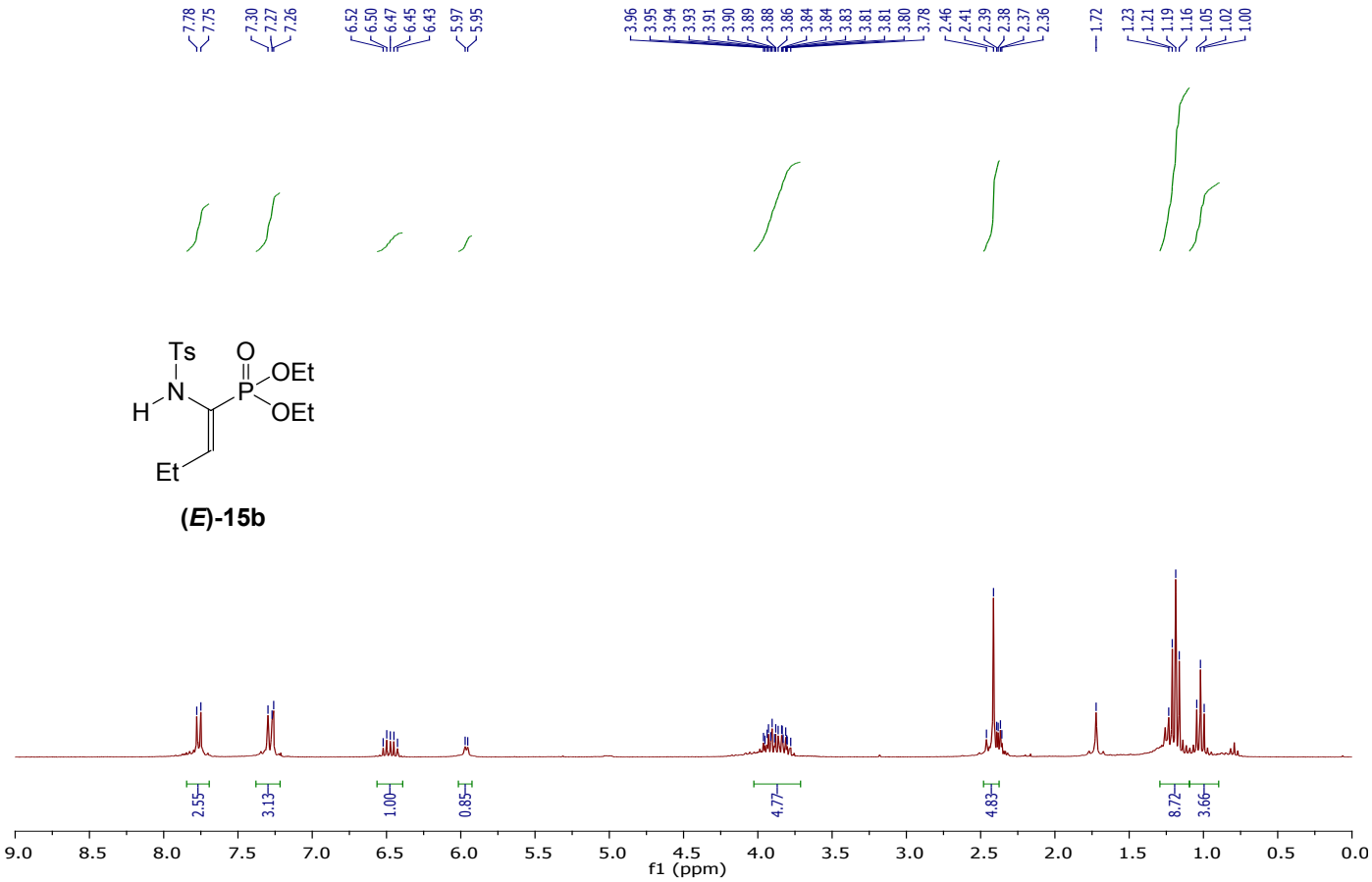
» ^{1}H NMR – 300 MHz – $CDCl_3$



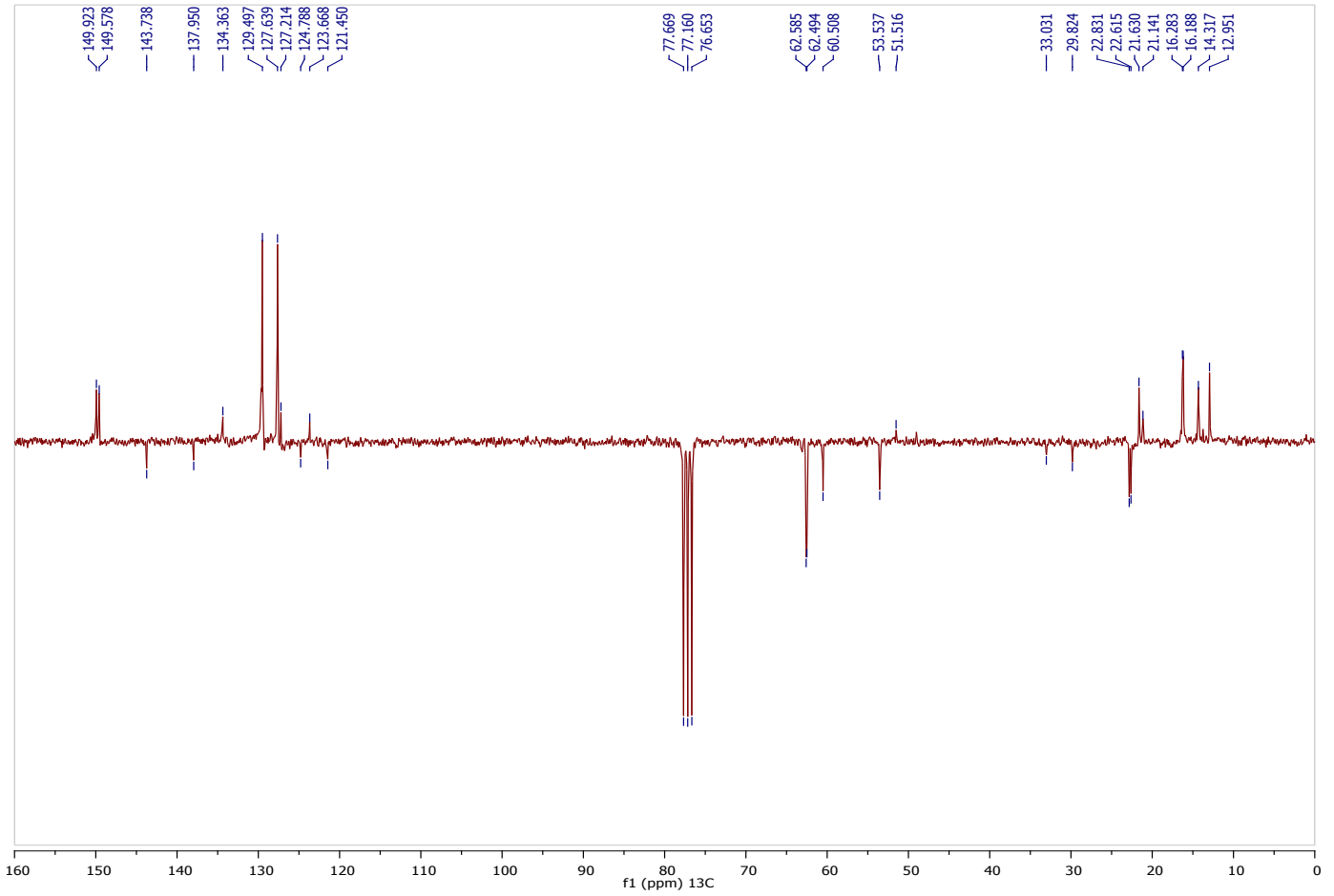
» ^{13}C NMR – 75 MHz – $CDCl_3$



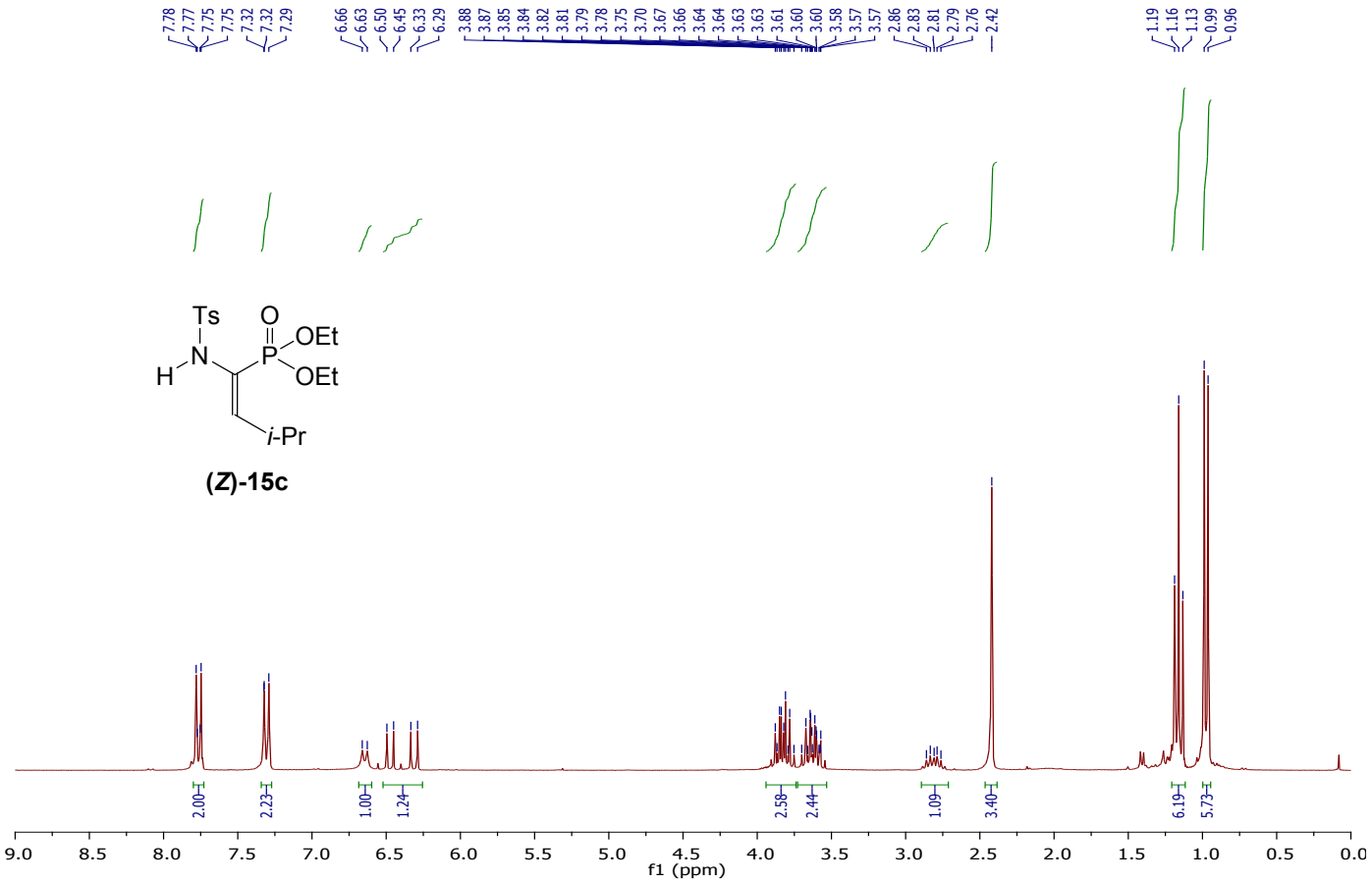
» ^{1}H NMR – 300 MHz – $CDCl_3$



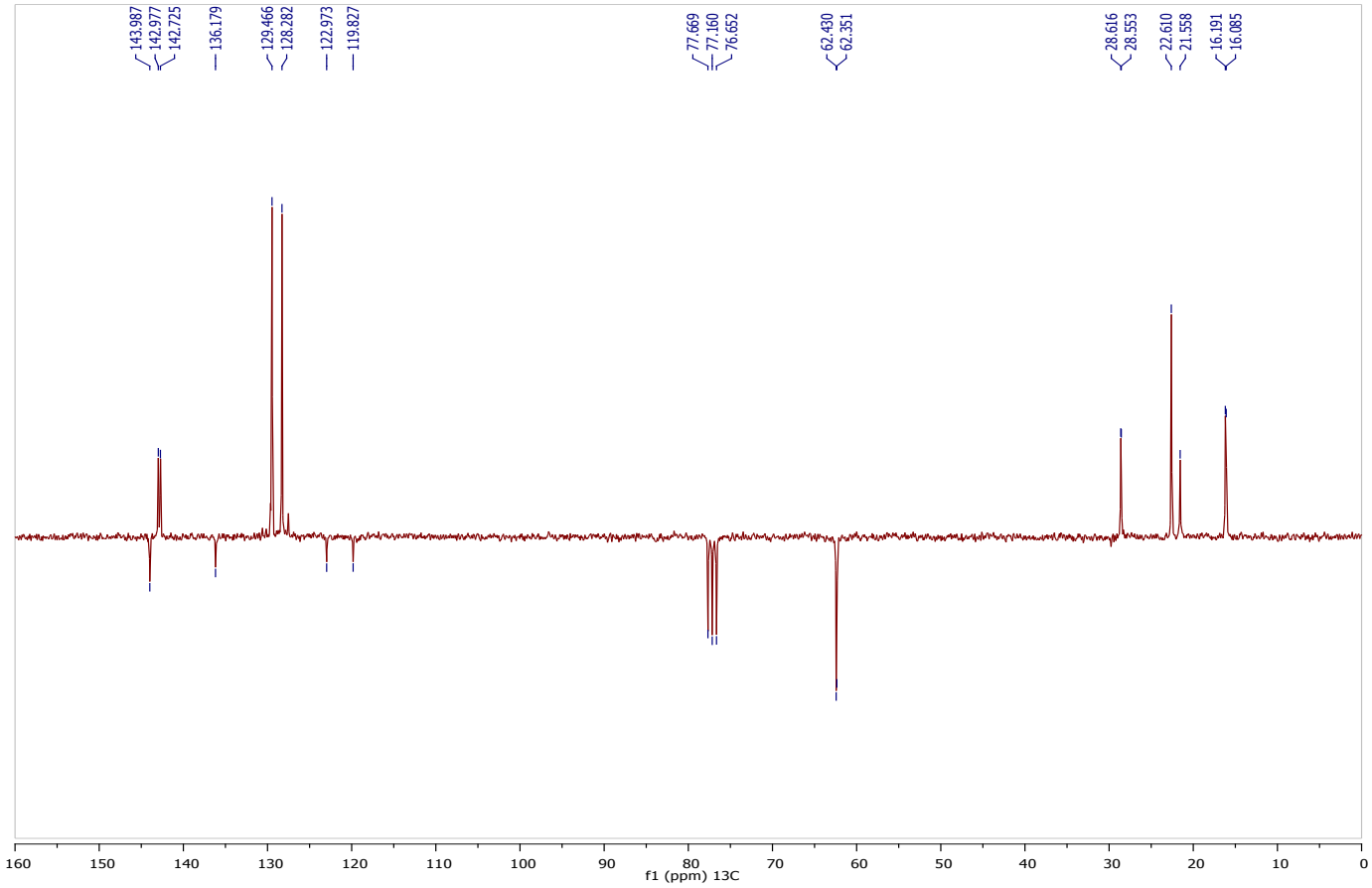
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



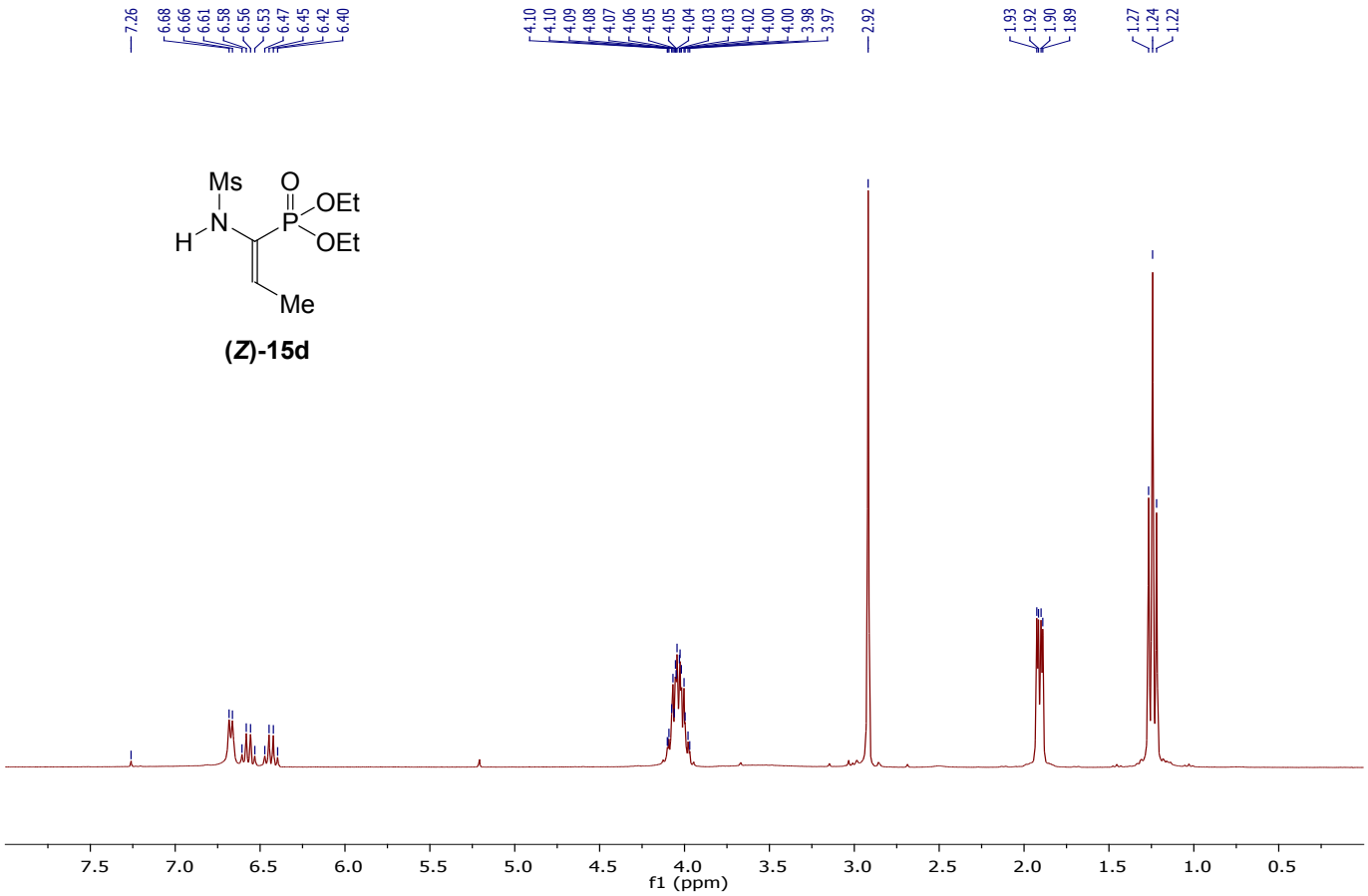
» ^{1}H NMR – 250 MHz – $CDCl_3$



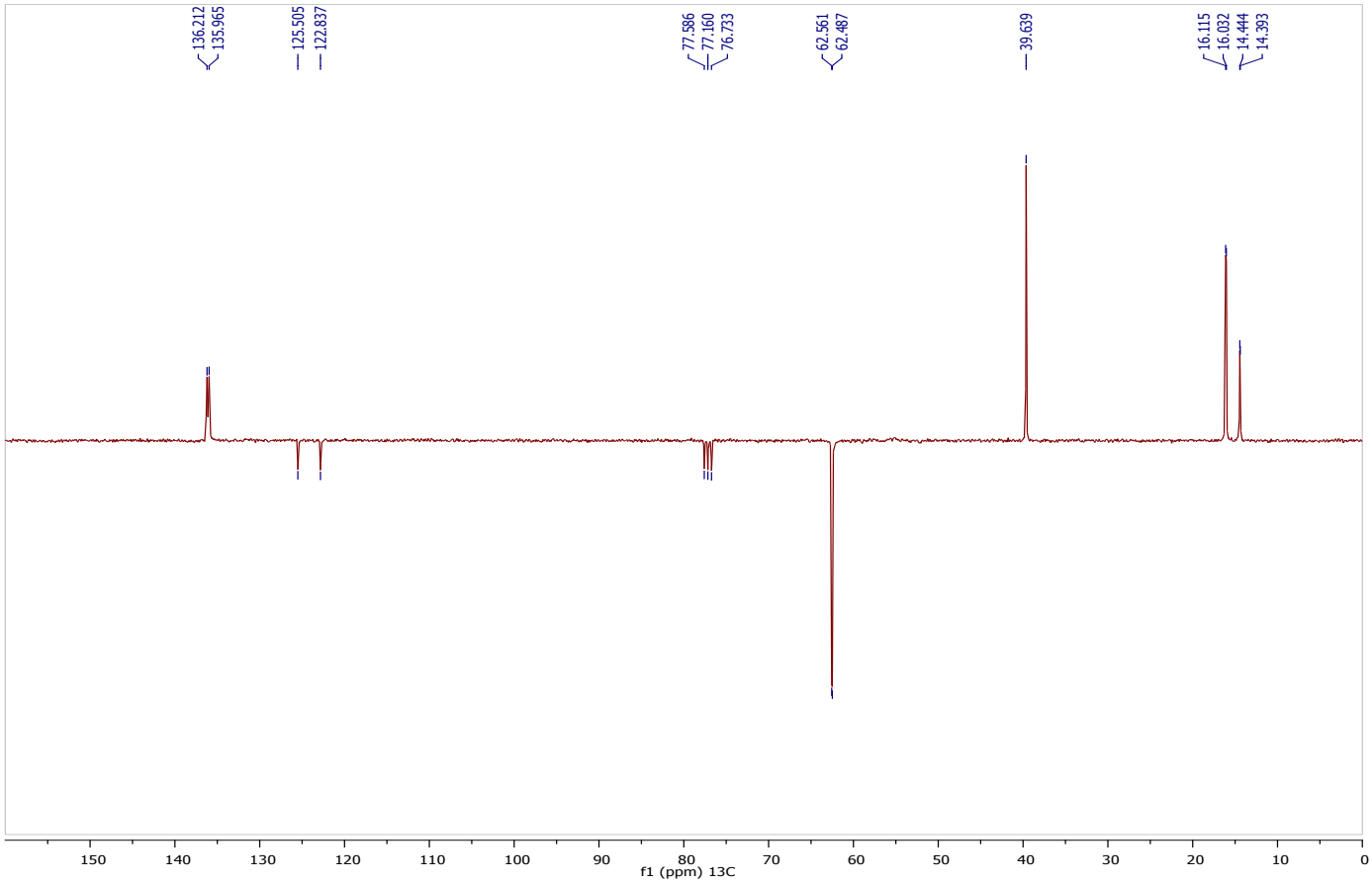
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



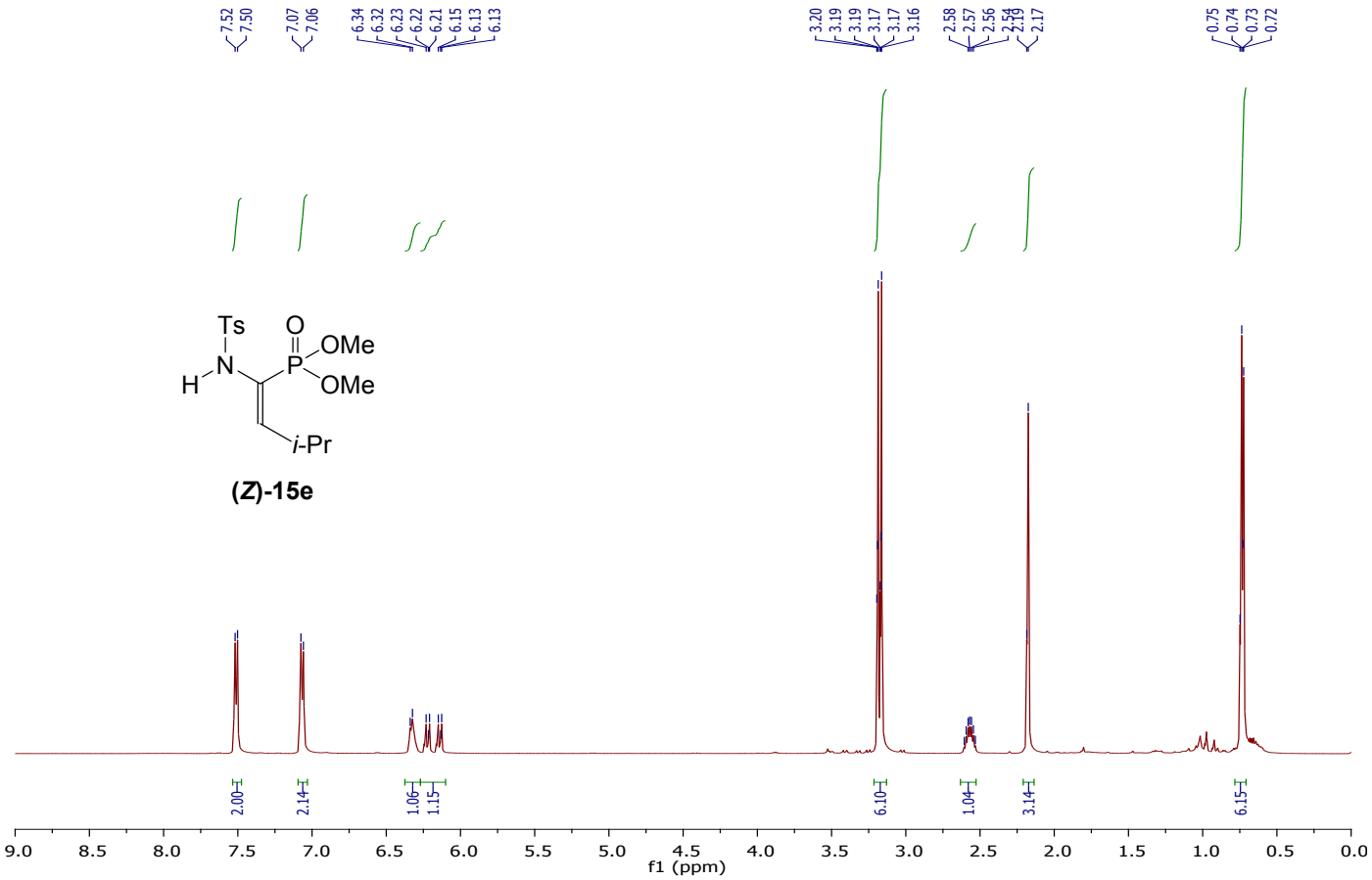
» ^{1}H NMR – 300 MHz – $CDCl_3$



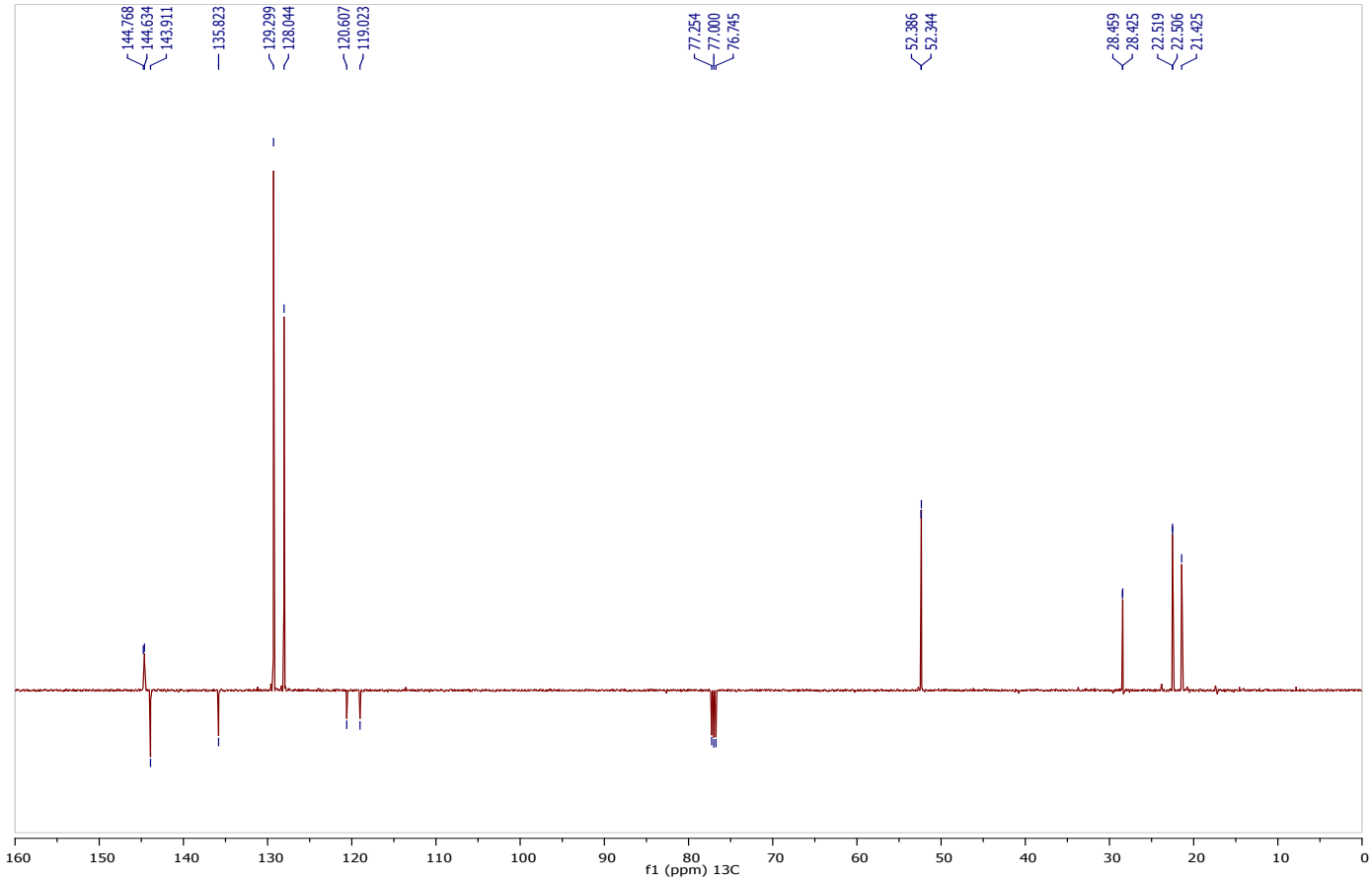
» ^{13}C NMR – 75 MHz – $CDCl_3$



» ^{1}H NMR – 500 MHz – $CDCl_3$

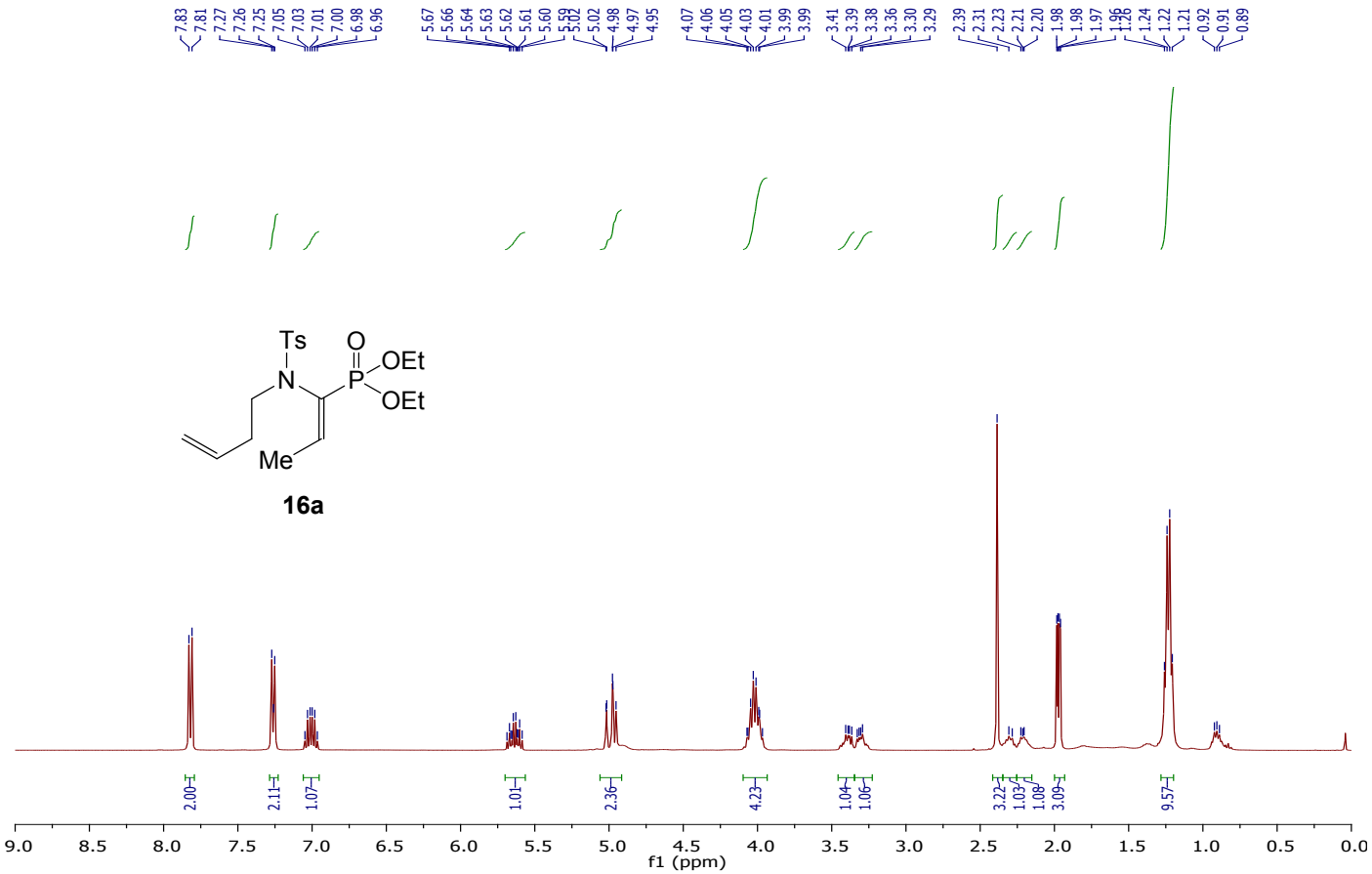


» ^{13}C NMR – 126 MHz – $CDCl_3$

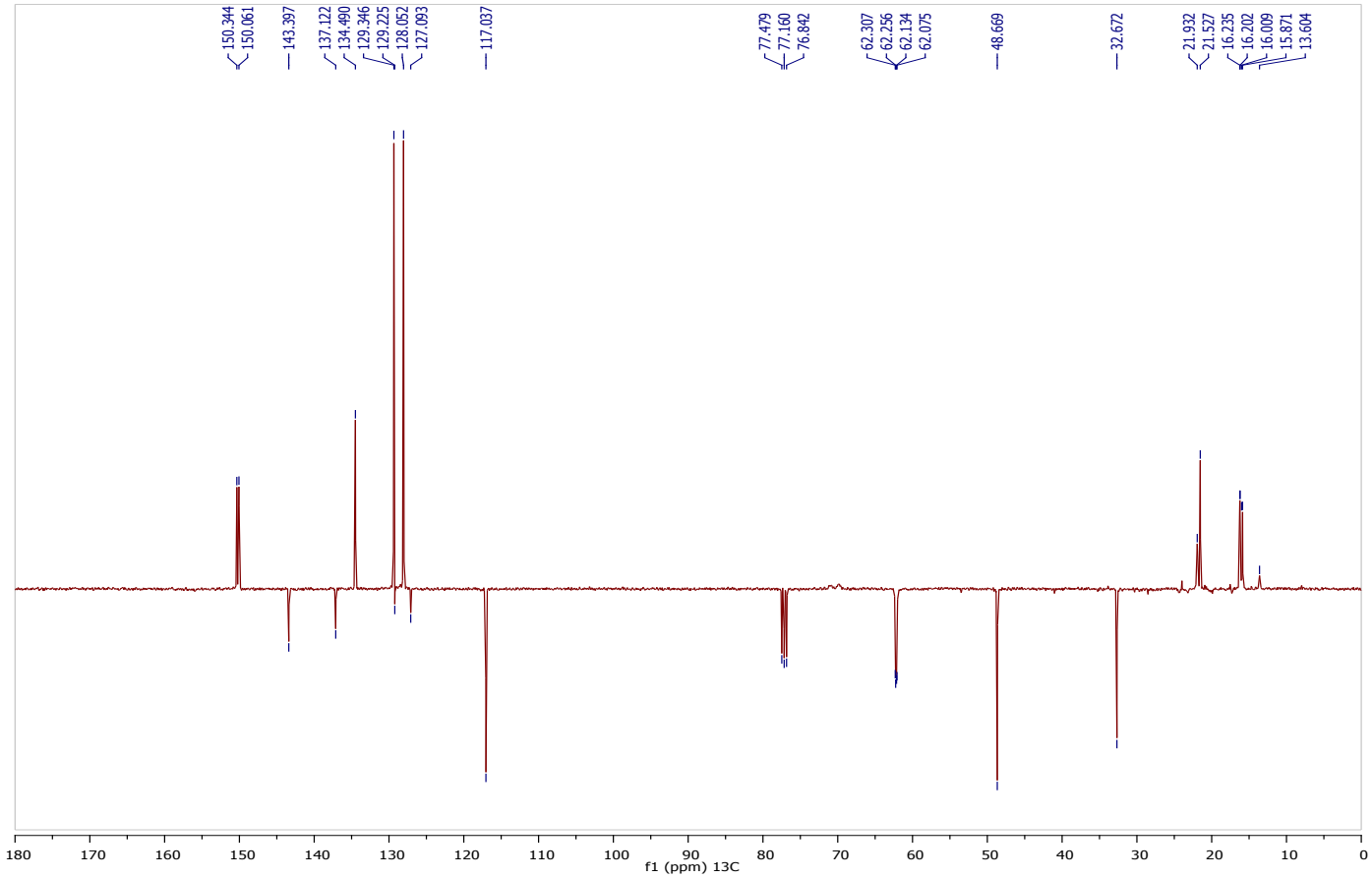


SPECTRA OF THE α-AVPS 16

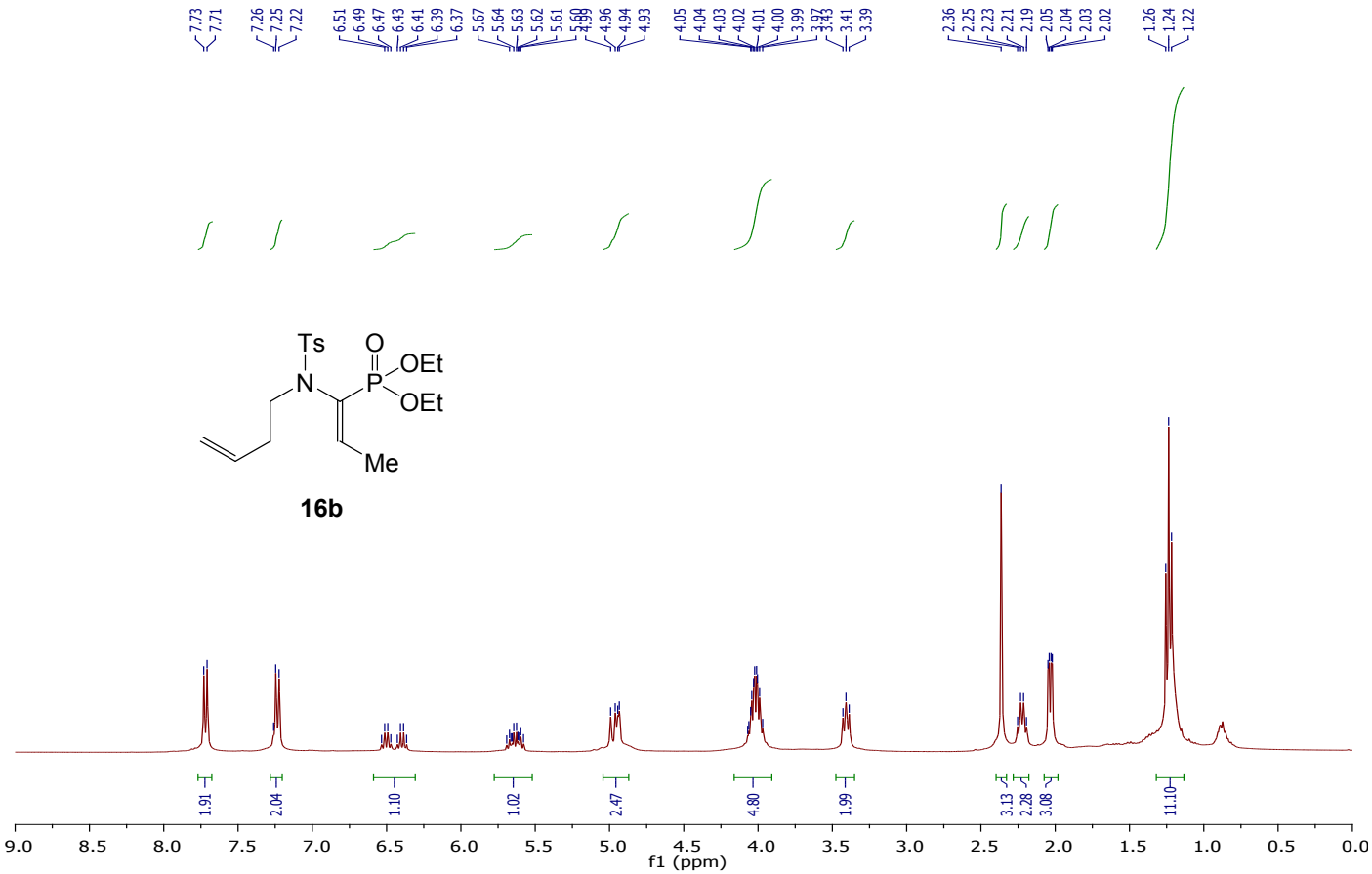
» ^{1}H NMR – 400 MHz – $CDCl_3$



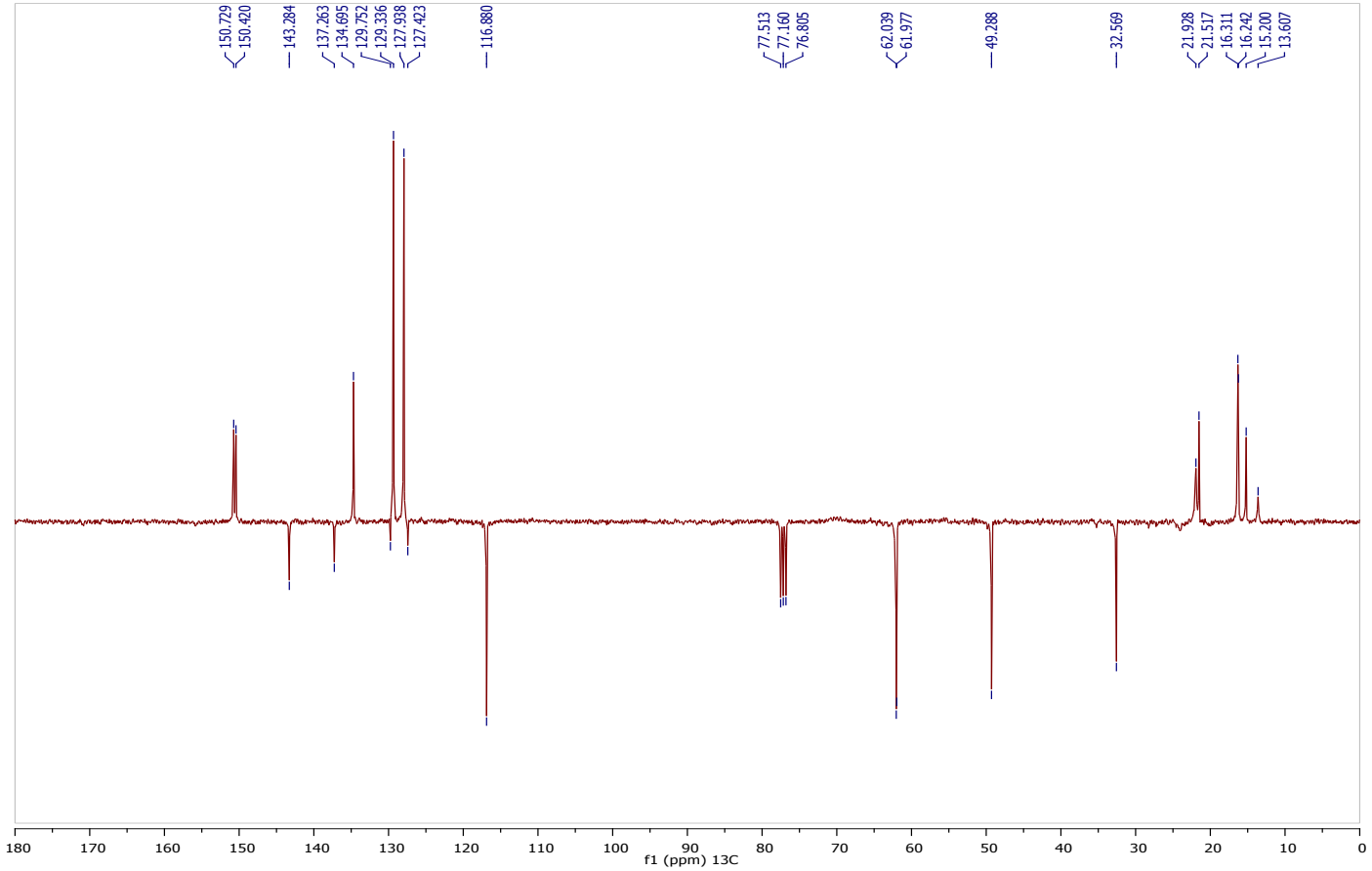
» ^{13}C NMR – 101 MHz – $CDCl_3$



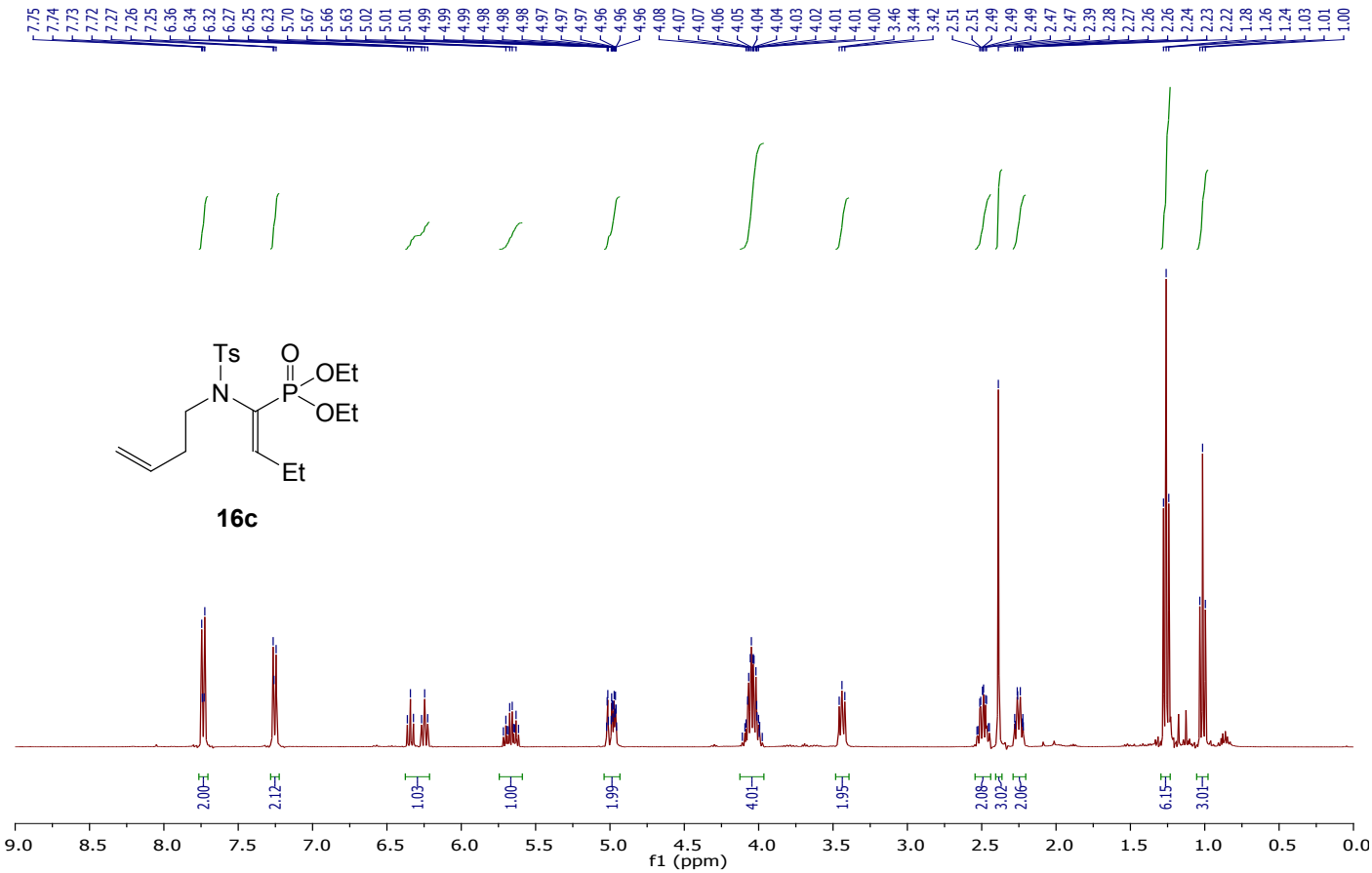
» ^{1}H NMR – 360 MHz – $CDCl_3$



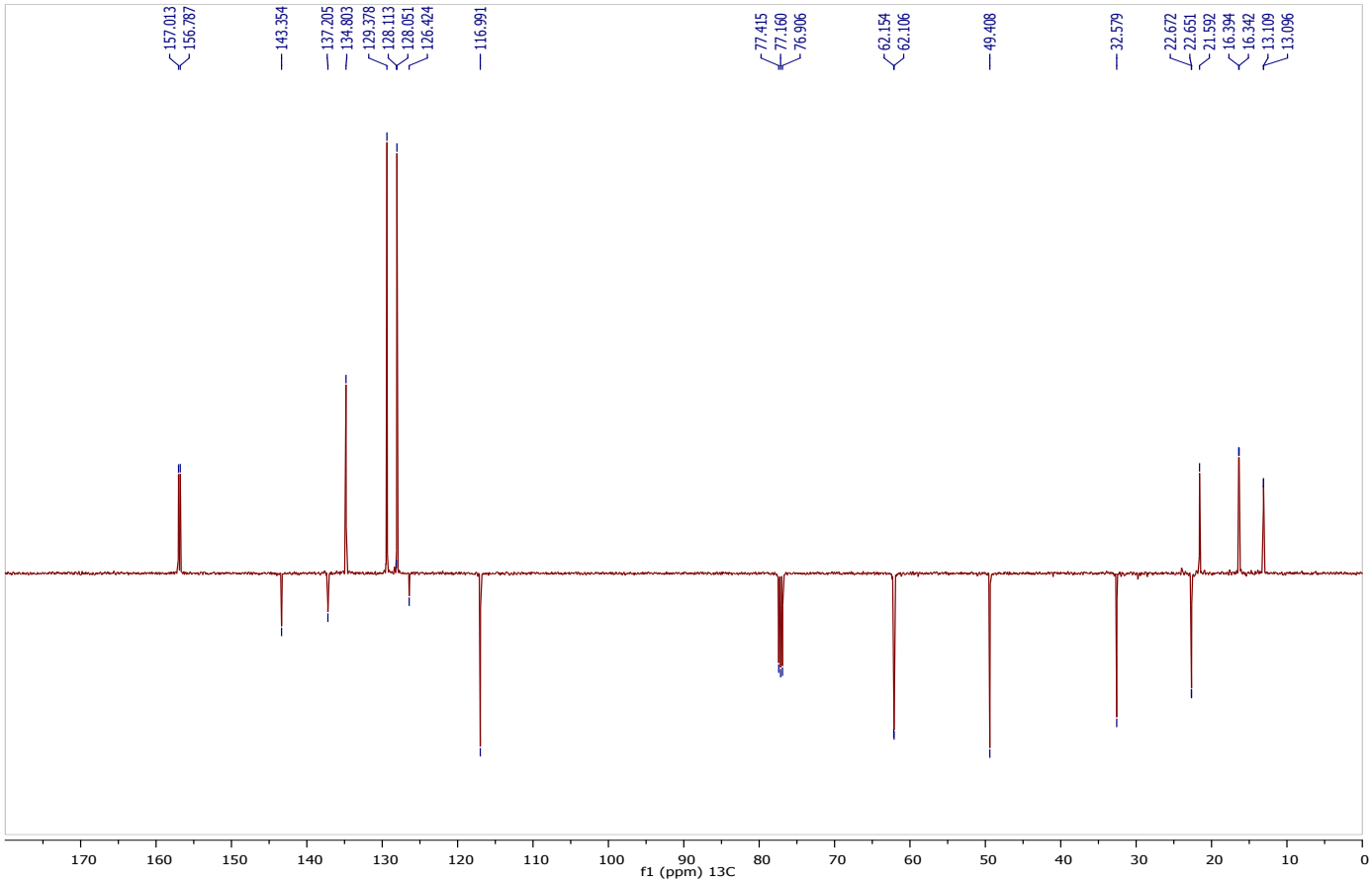
» ^{13}C NMR – 91 MHz – $CDCl_3$



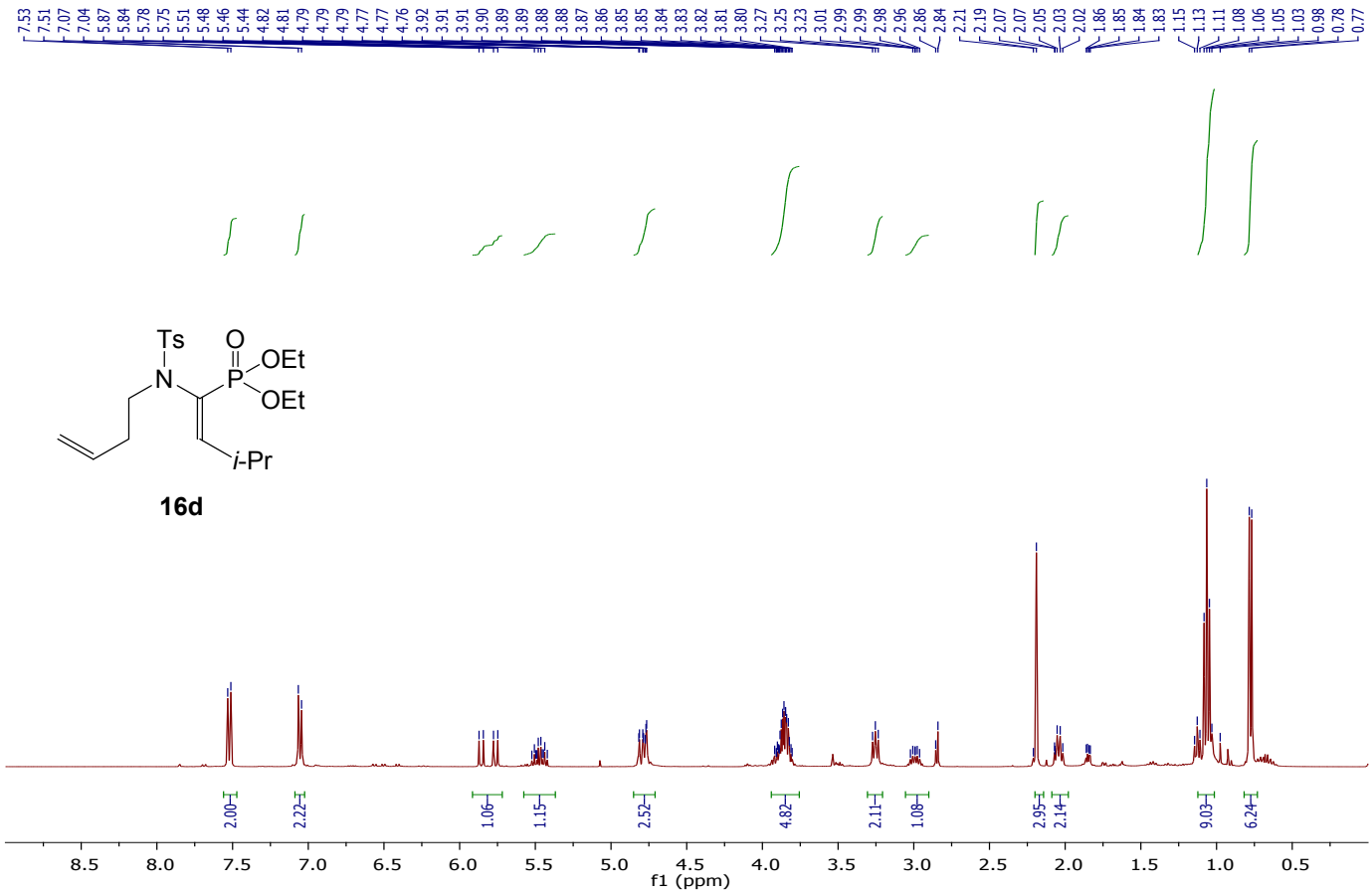
» ^{1}H NMR – 400 MHz – $CDCl_3$



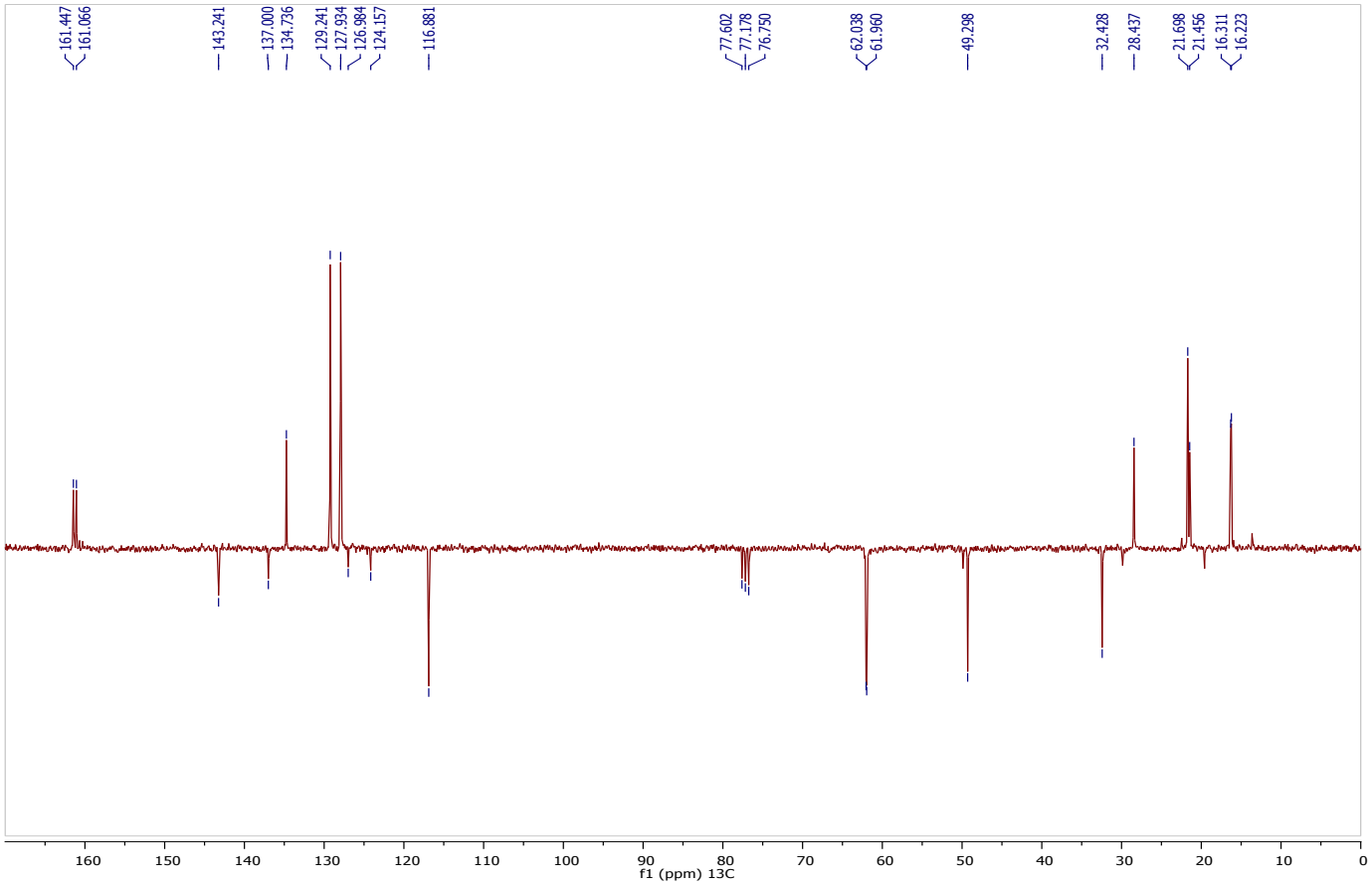
» ^{13}C NMR – 126 MHz – $CDCl_3$



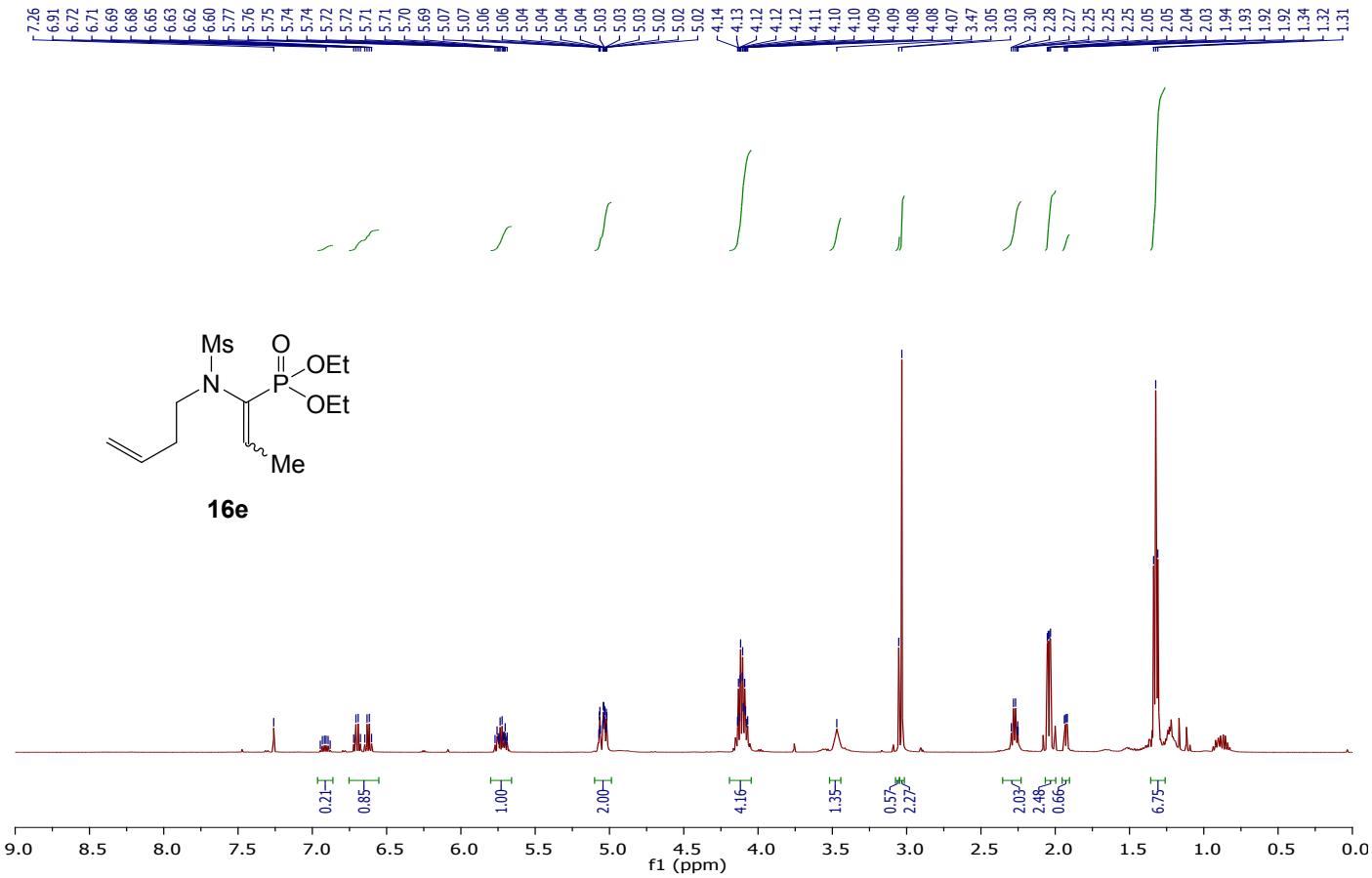
» ^{1}H NMR – 400 MHz – $CDCl_3$



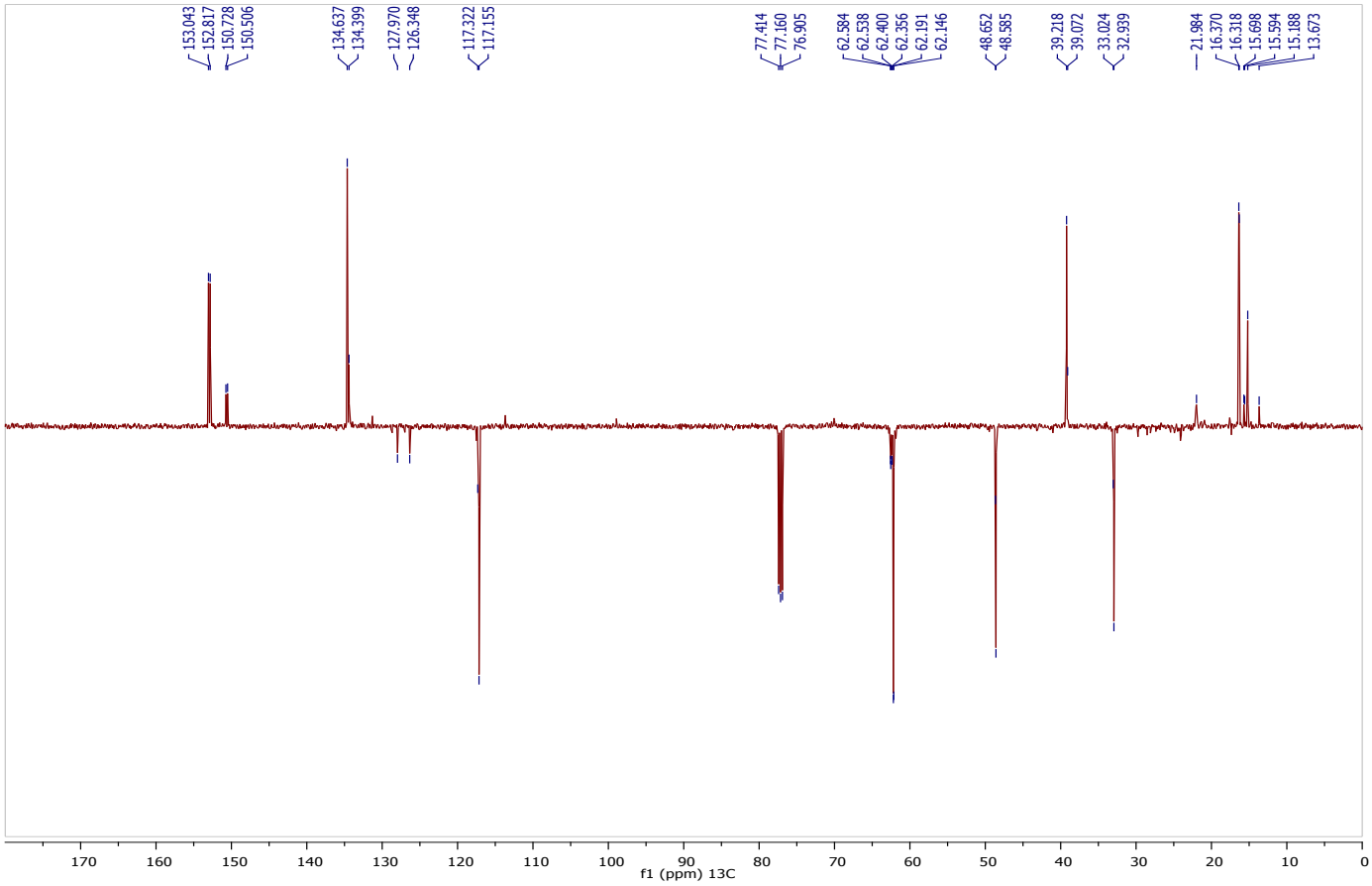
» ^{13}C NMR – 126 MHz – $CDCl_3$



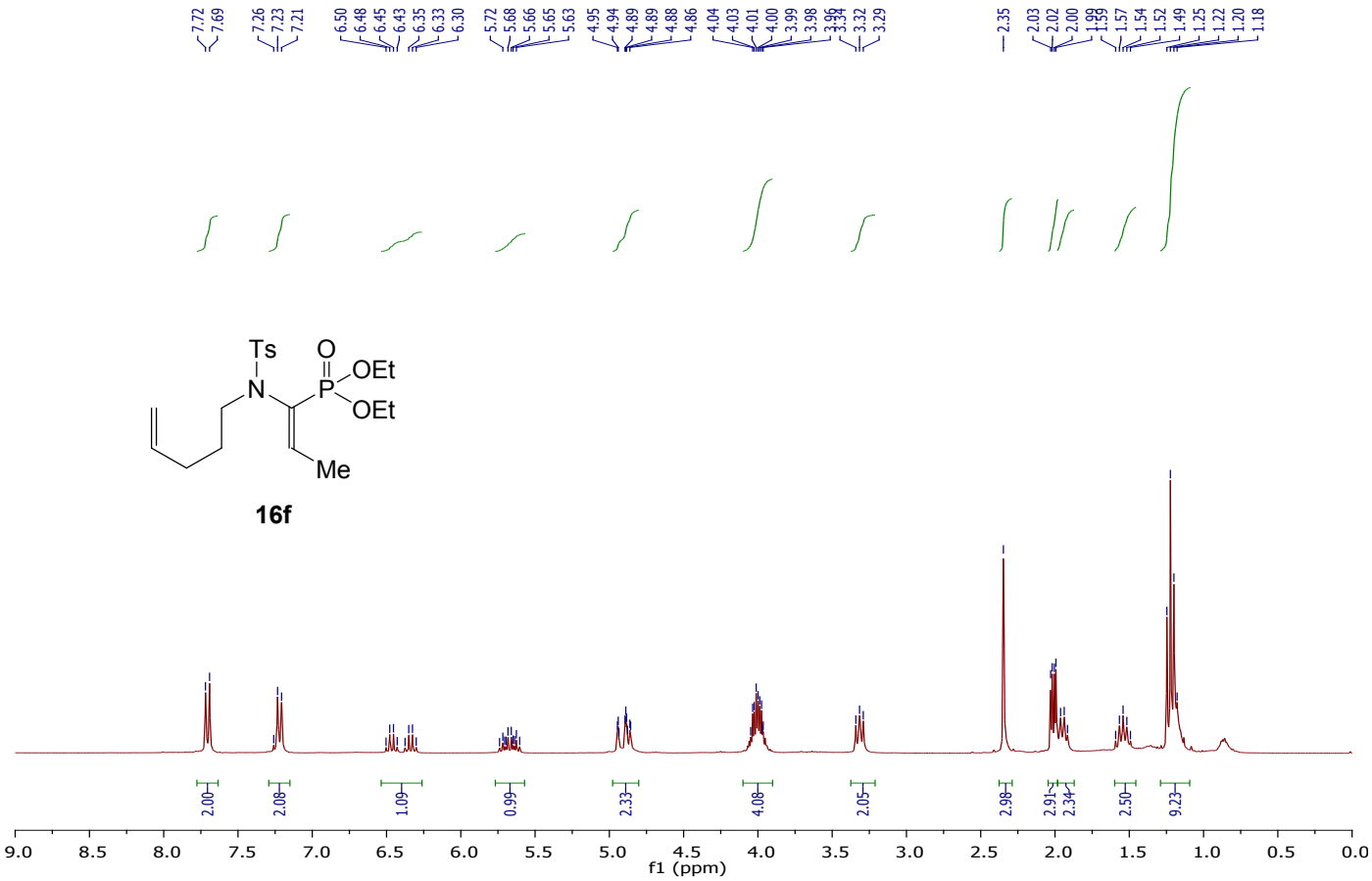
» ^{1}H NMR – 500 MHz – $CDCl_3$



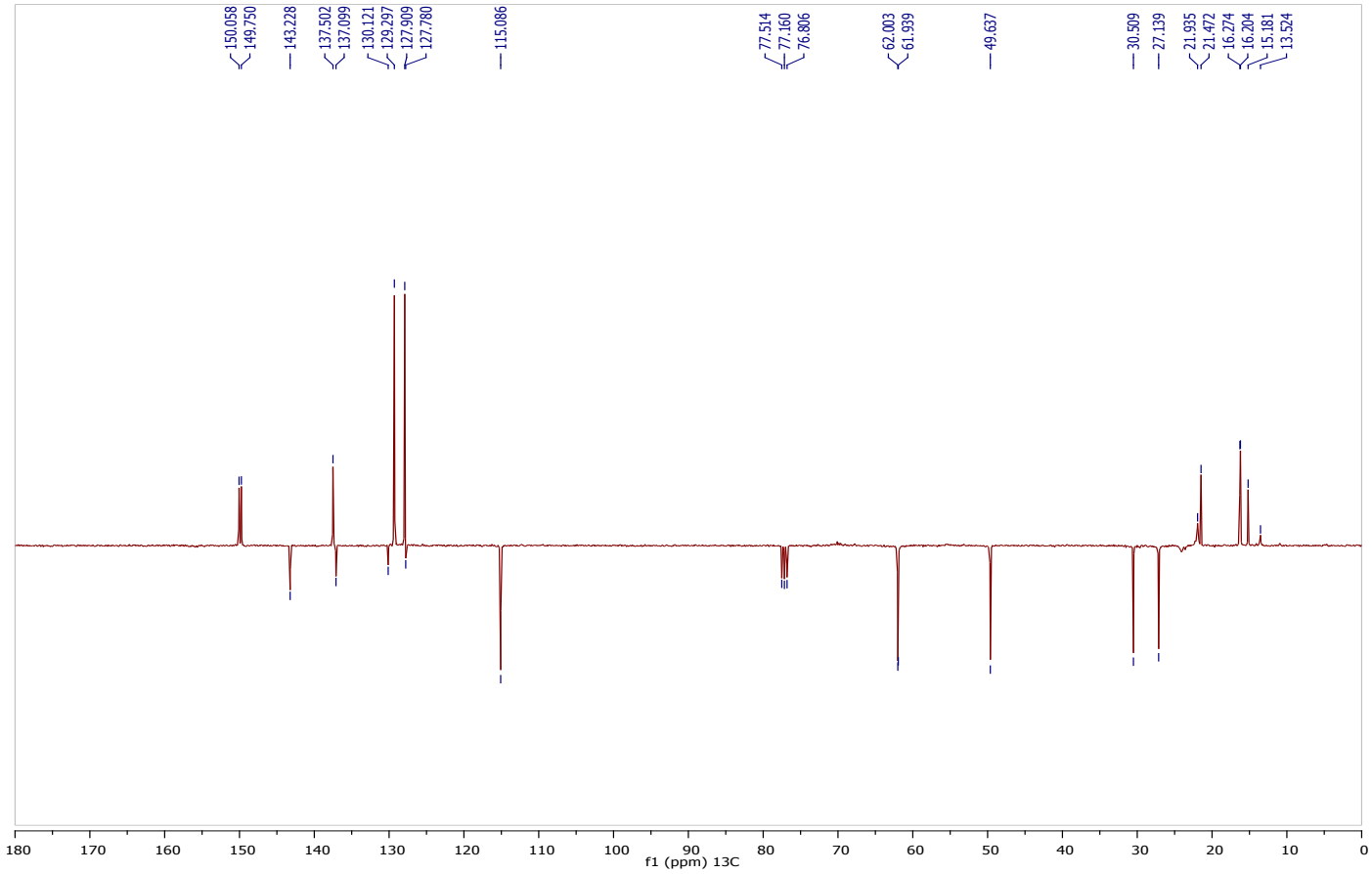
» ^{13}C NMR – 126 MHz – $CDCl_3$



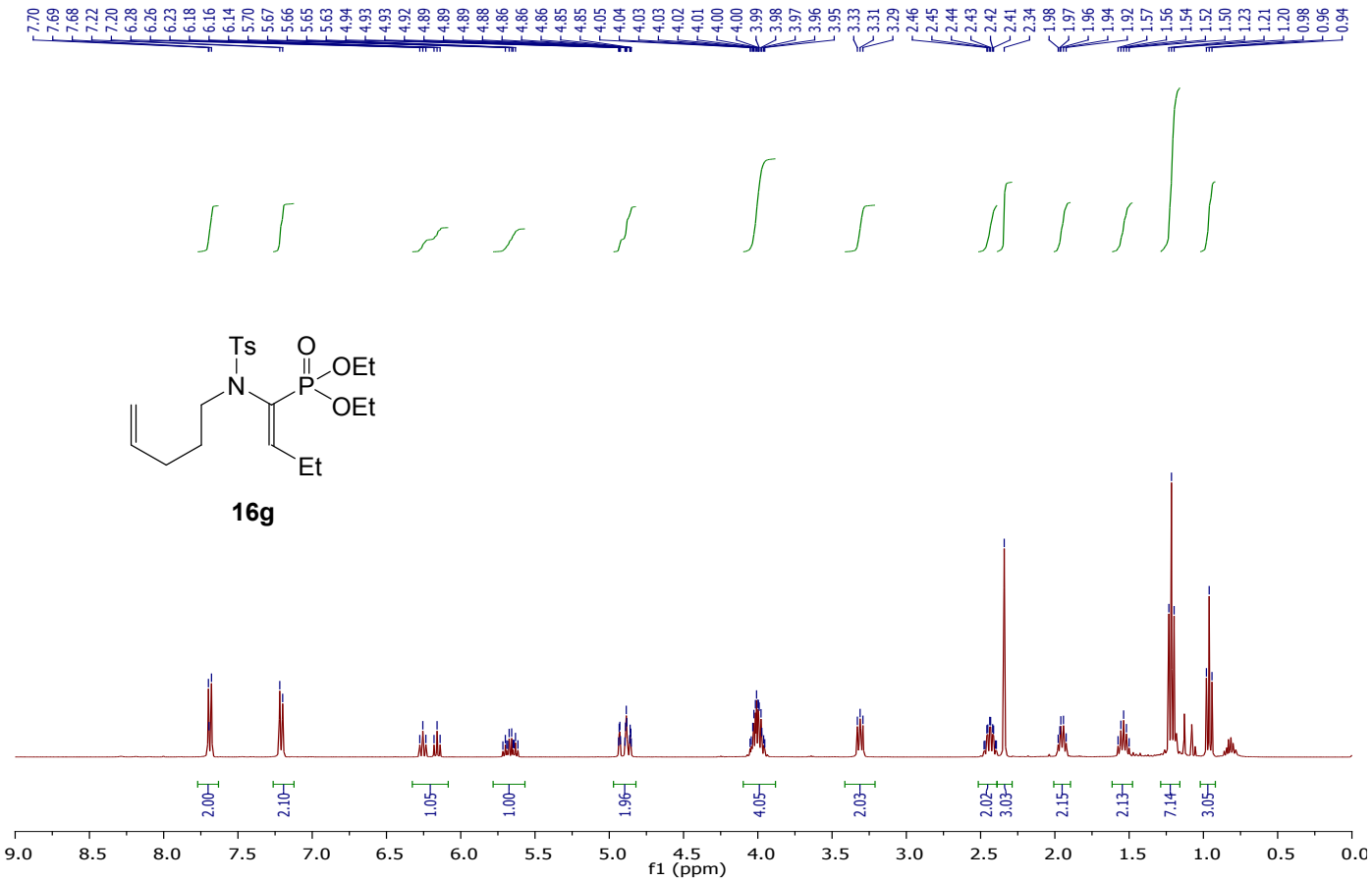
» ^{1}H NMR – 300 MHz – $CDCl_3$



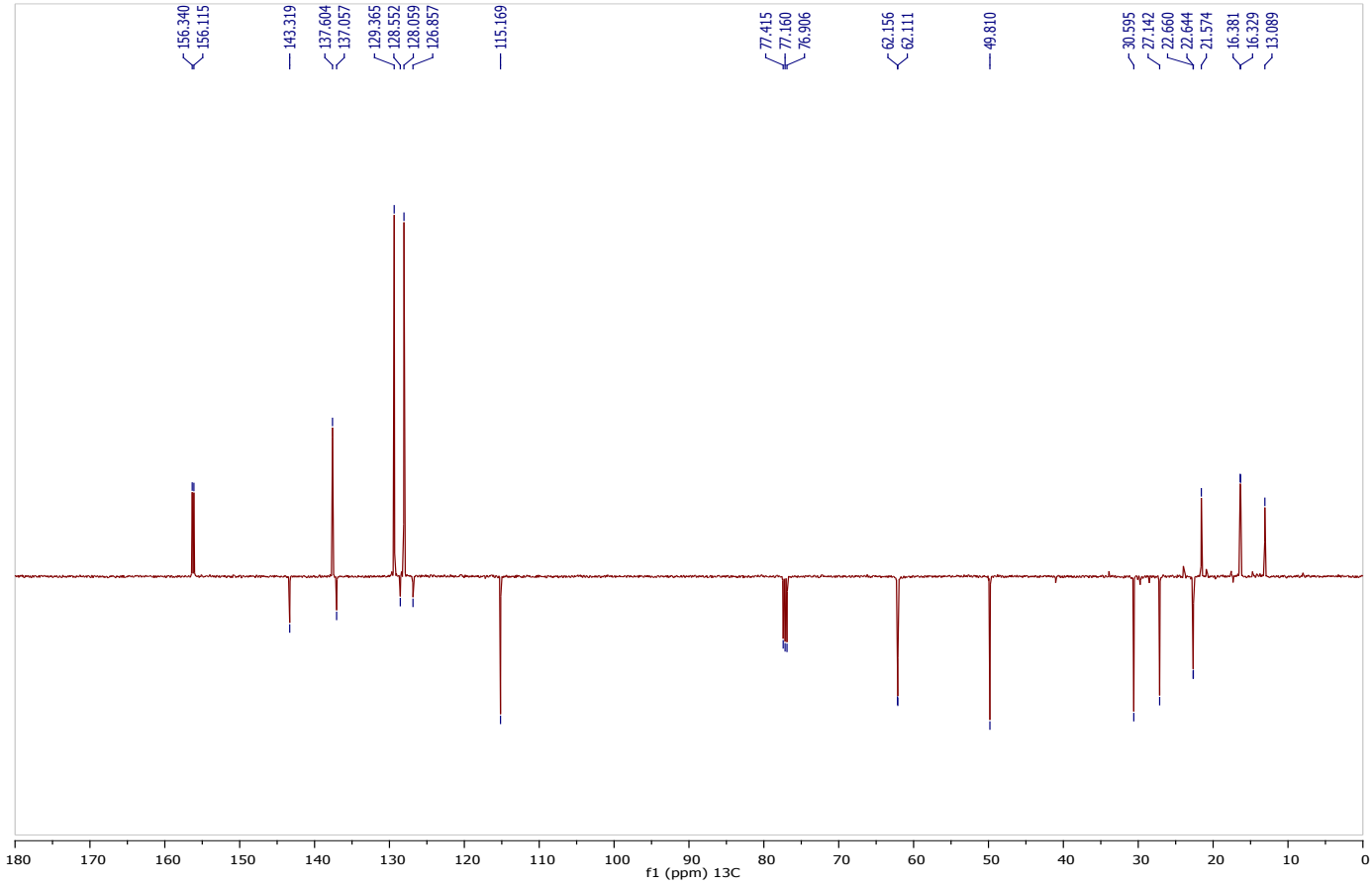
» ^{13}C NMR – 91 MHz – $CDCl_3$



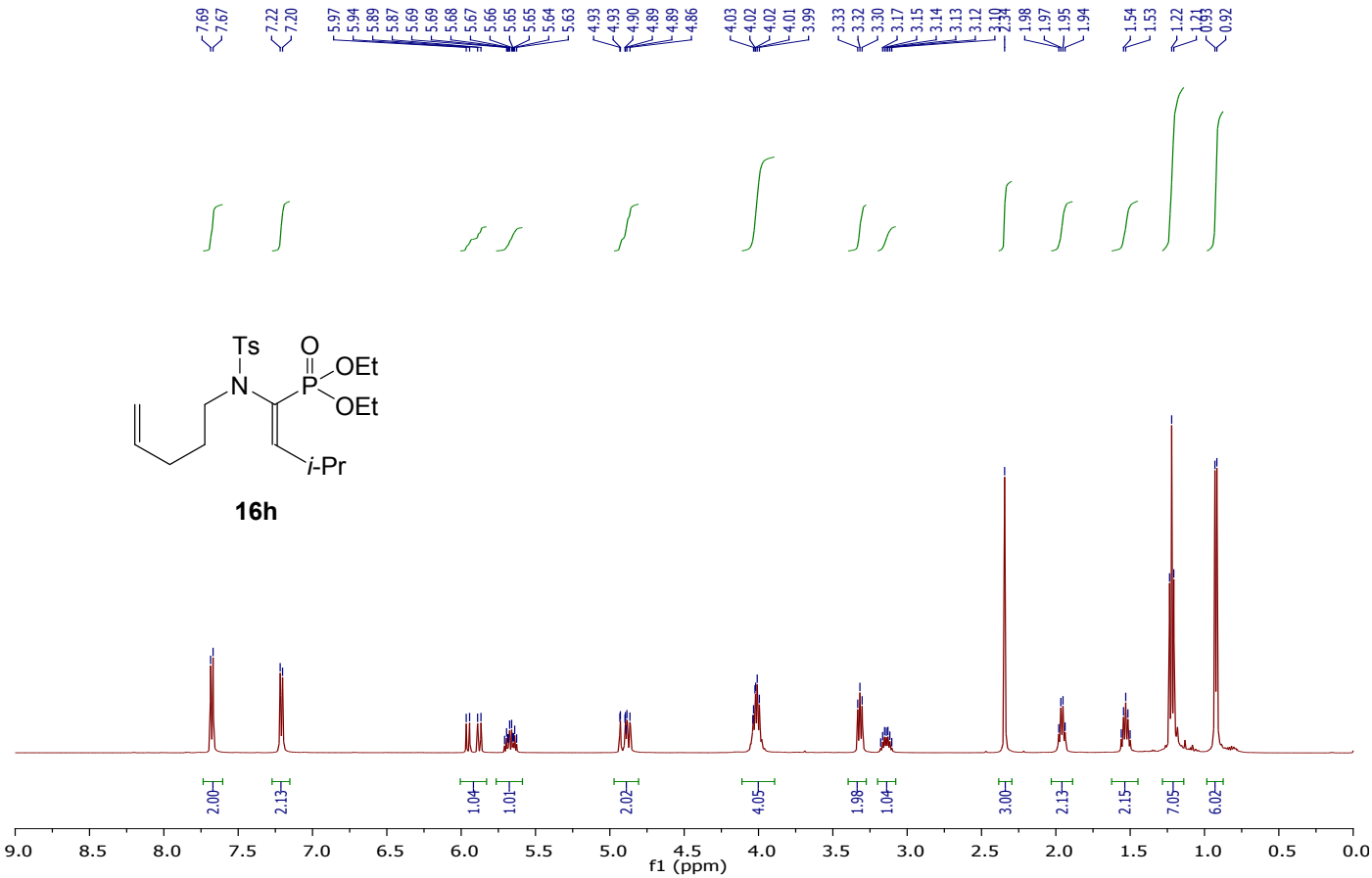
» ^{1}H NMR – 400 MHz – $CDCl_3$



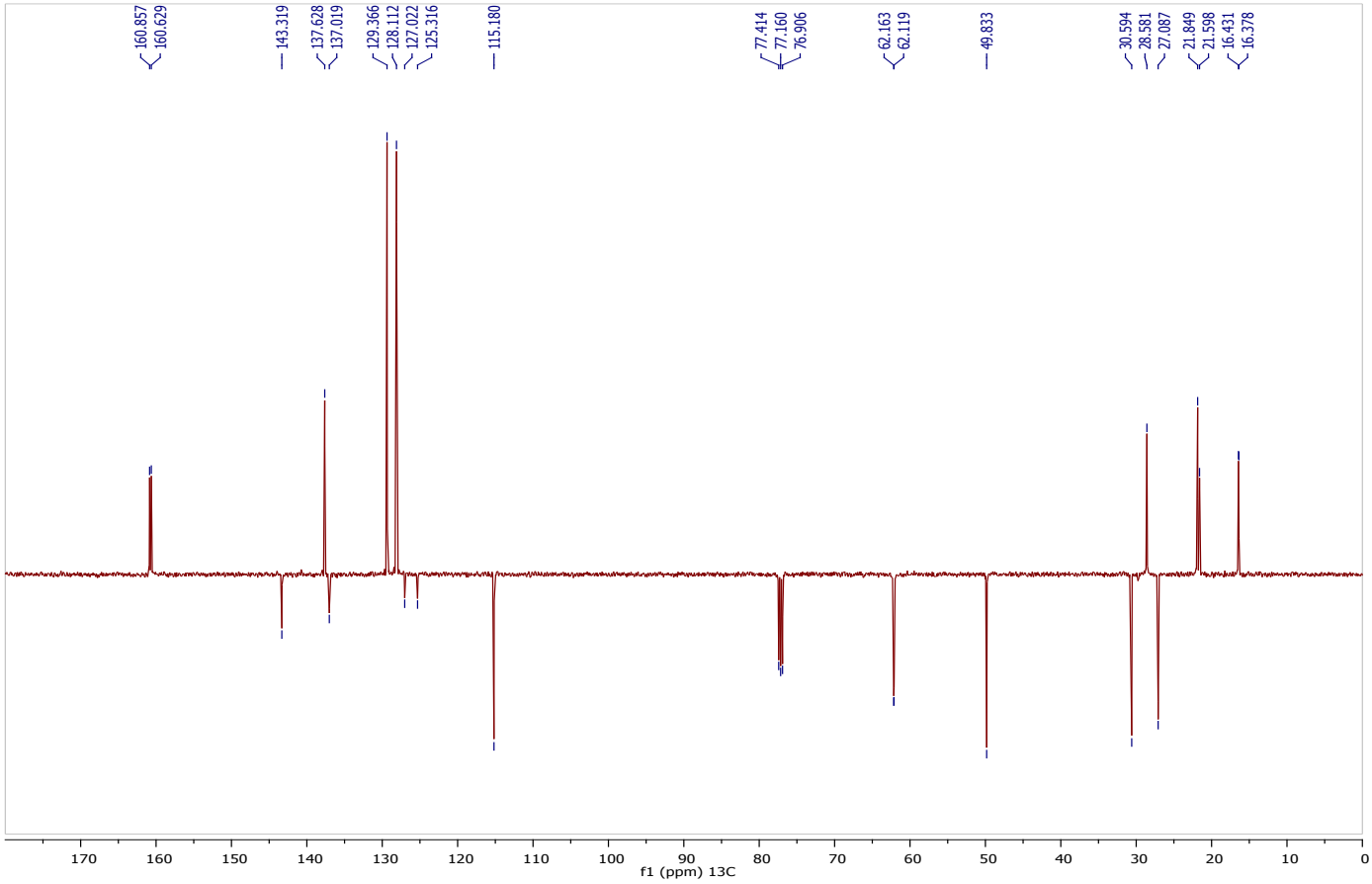
» ^{13}C NMR – 126 MHz – $CDCl_3$



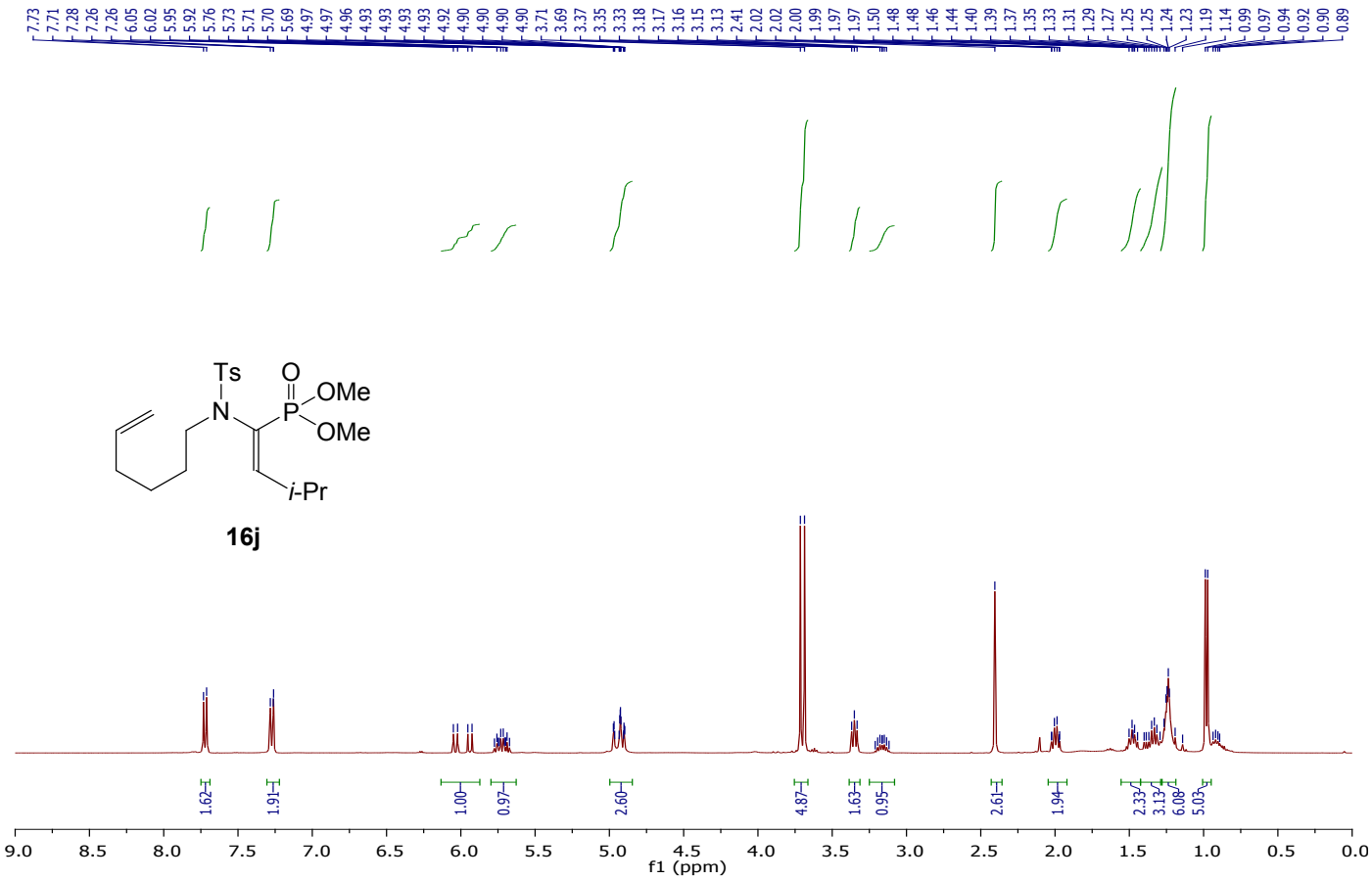
» ^{1}H NMR – 500 MHz – $CDCl_3$



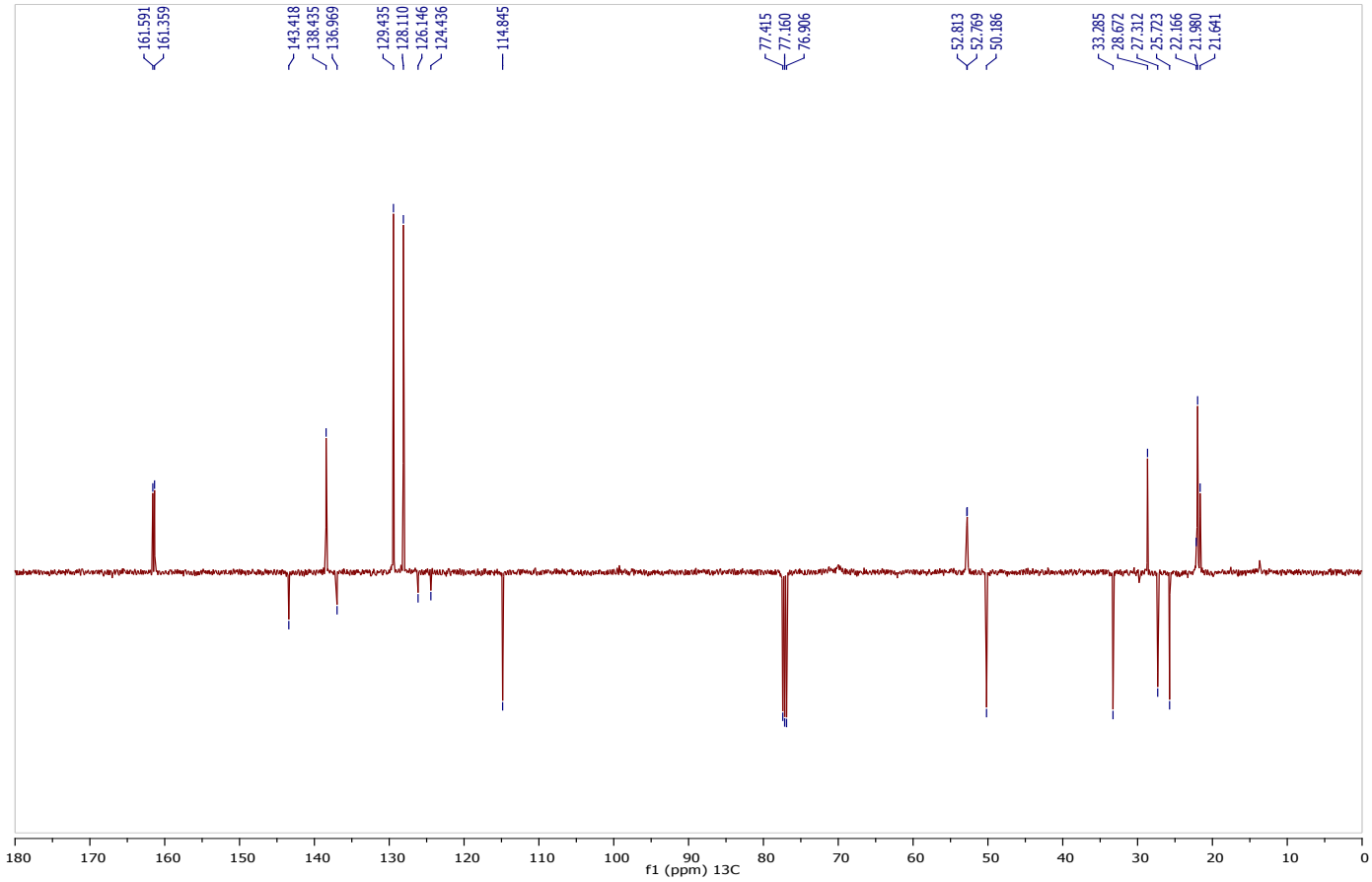
» ^{13}C NMR – 126 MHz – $CDCl_3$



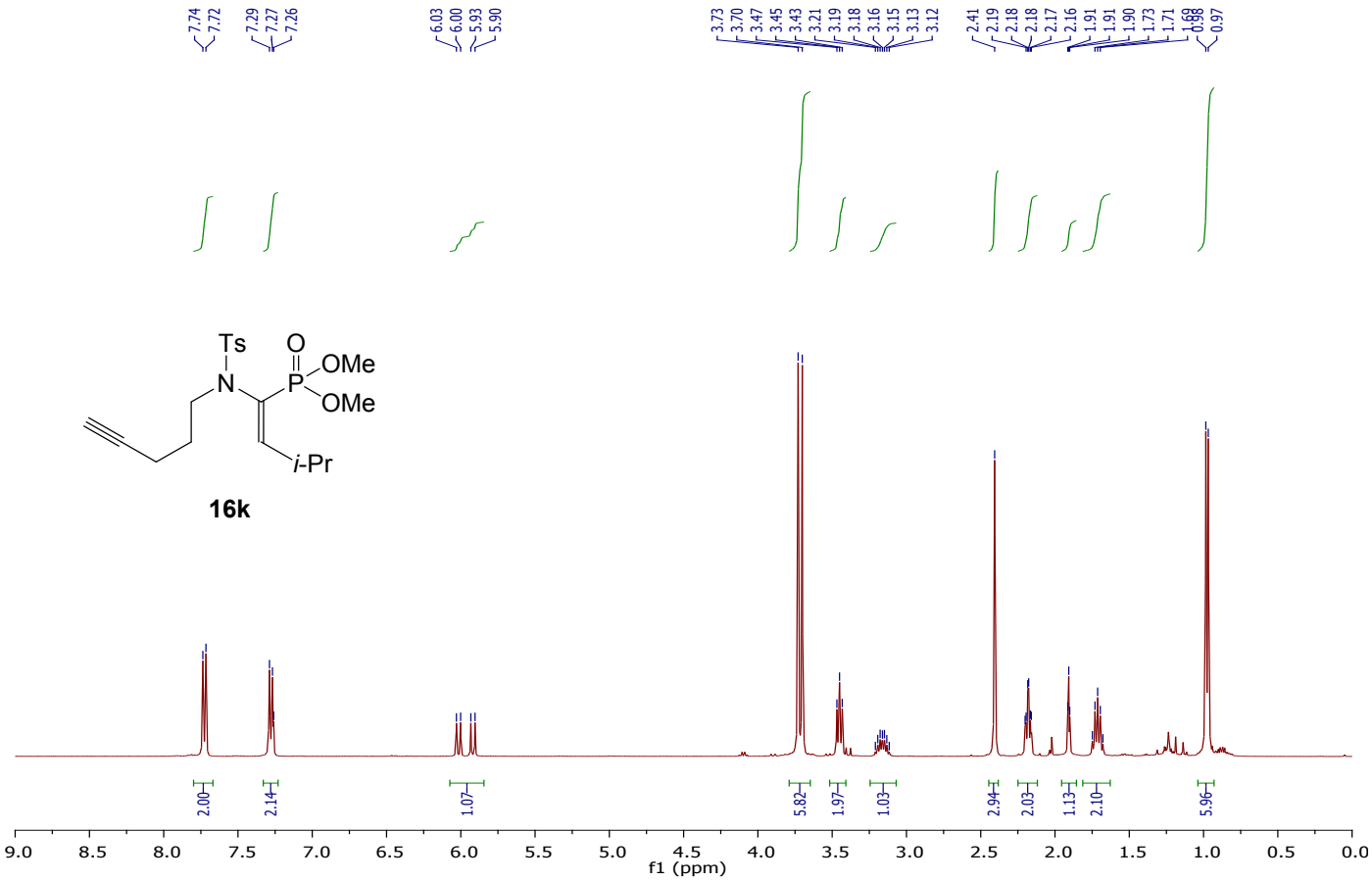
» ^{1}H NMR – 400 MHz – $CDCl_3$



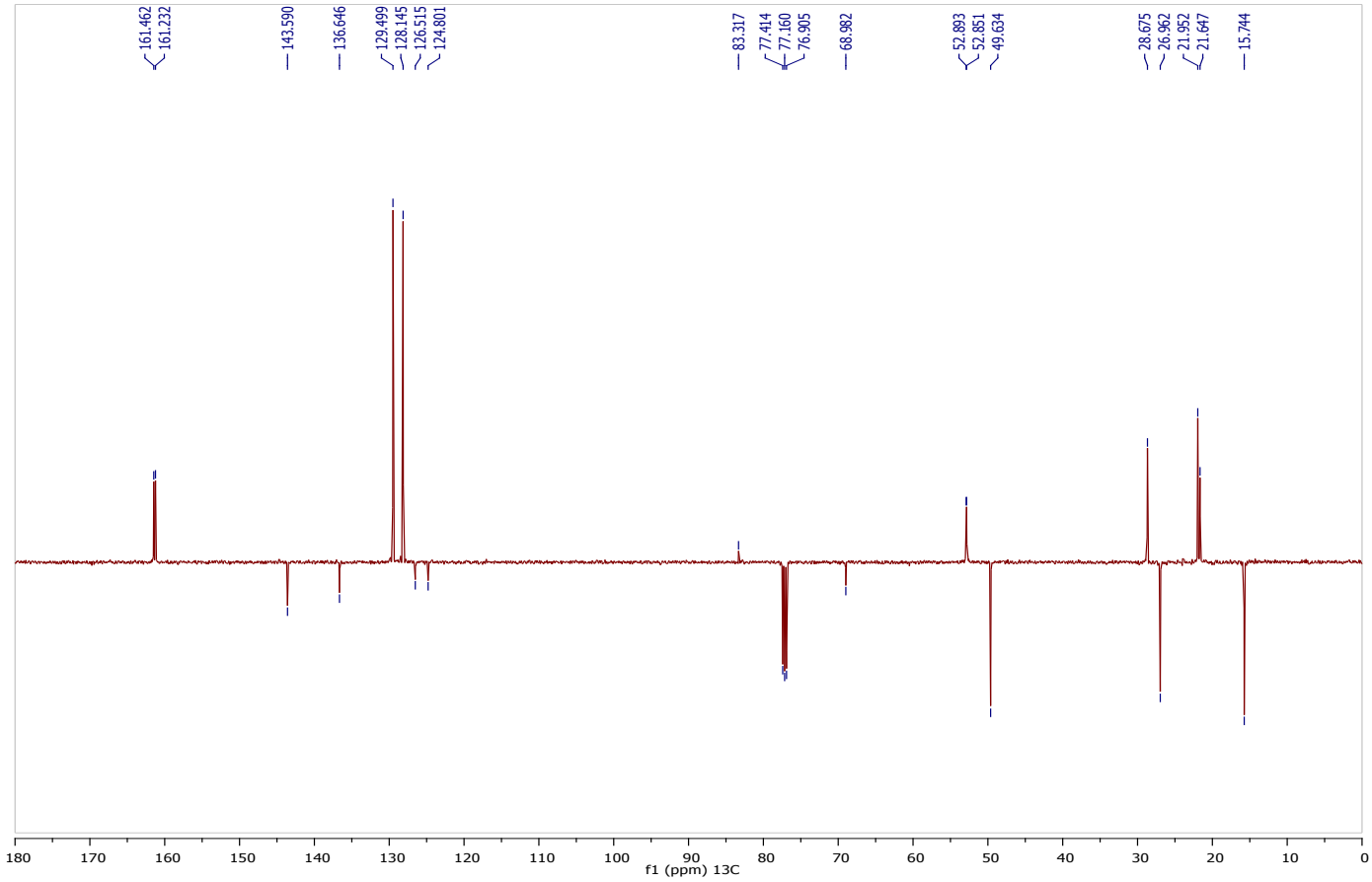
» ^{13}C NMR – 126 MHz – $CDCl_3$



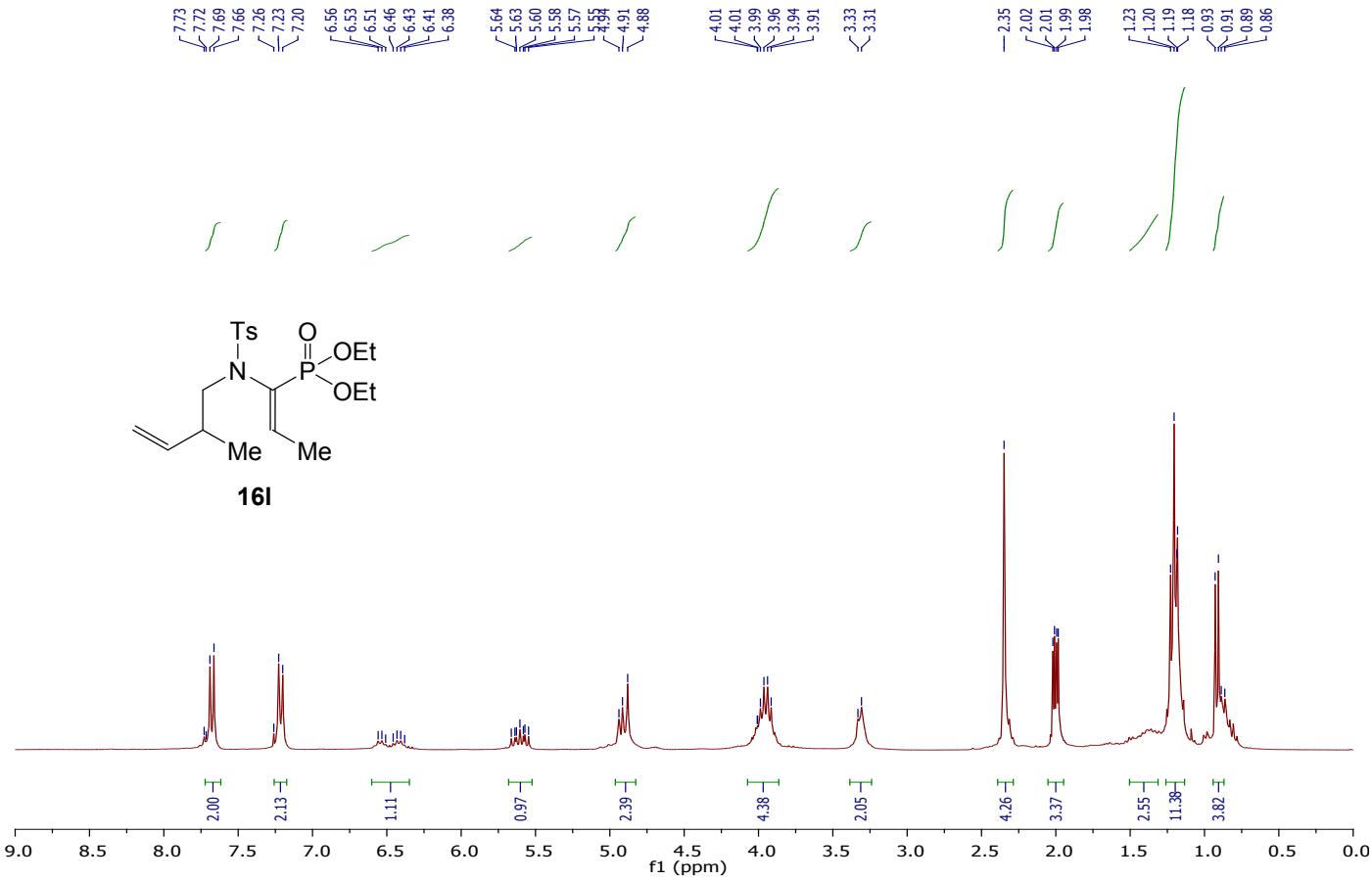
» ^{1}H NMR – 400 MHz – $CDCl_3$



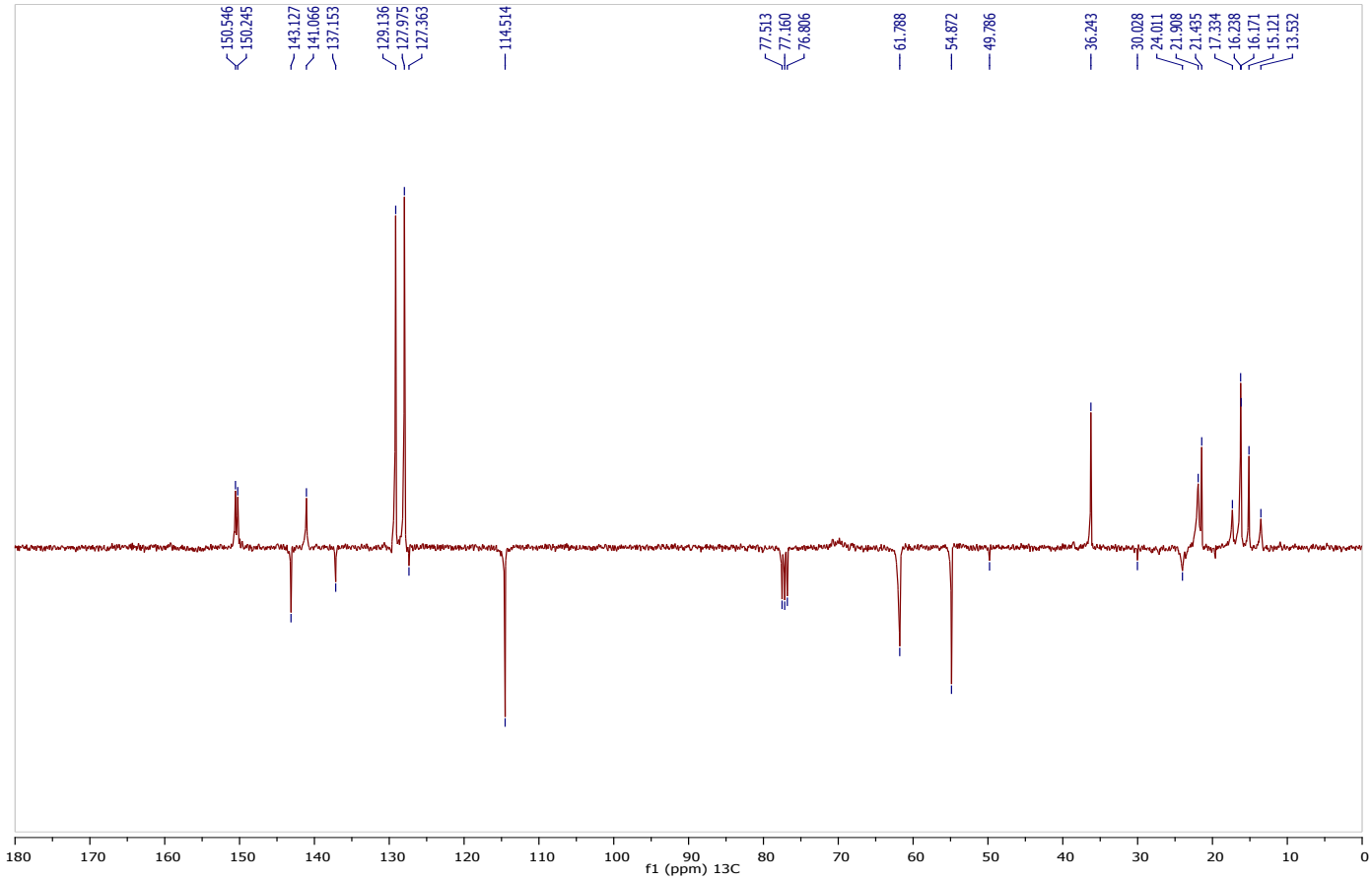
» ^{13}C NMR – 126 MHz – $CDCl_3$



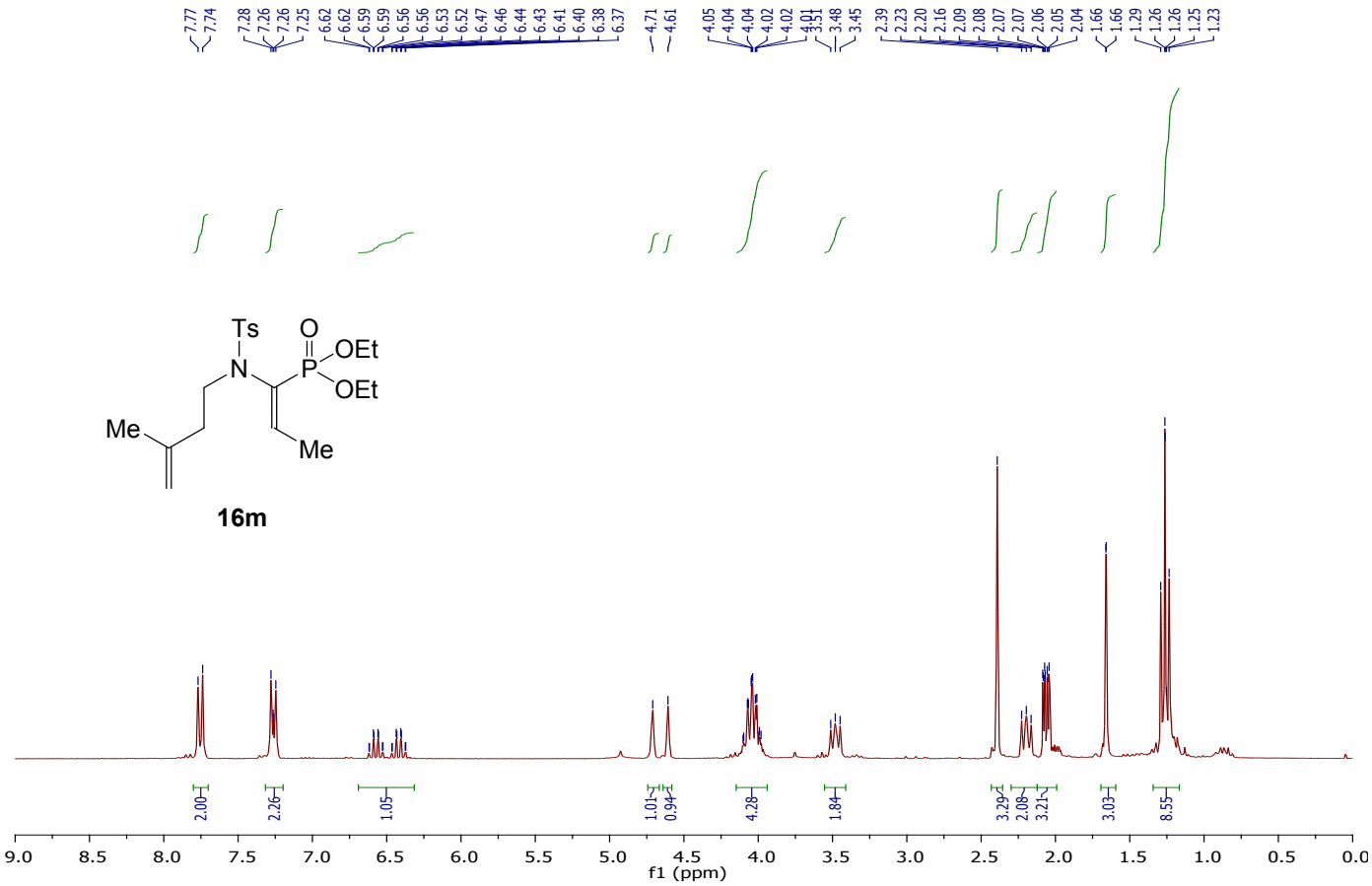
» ^{1}H NMR – 300 MHz – $CDCl_3$



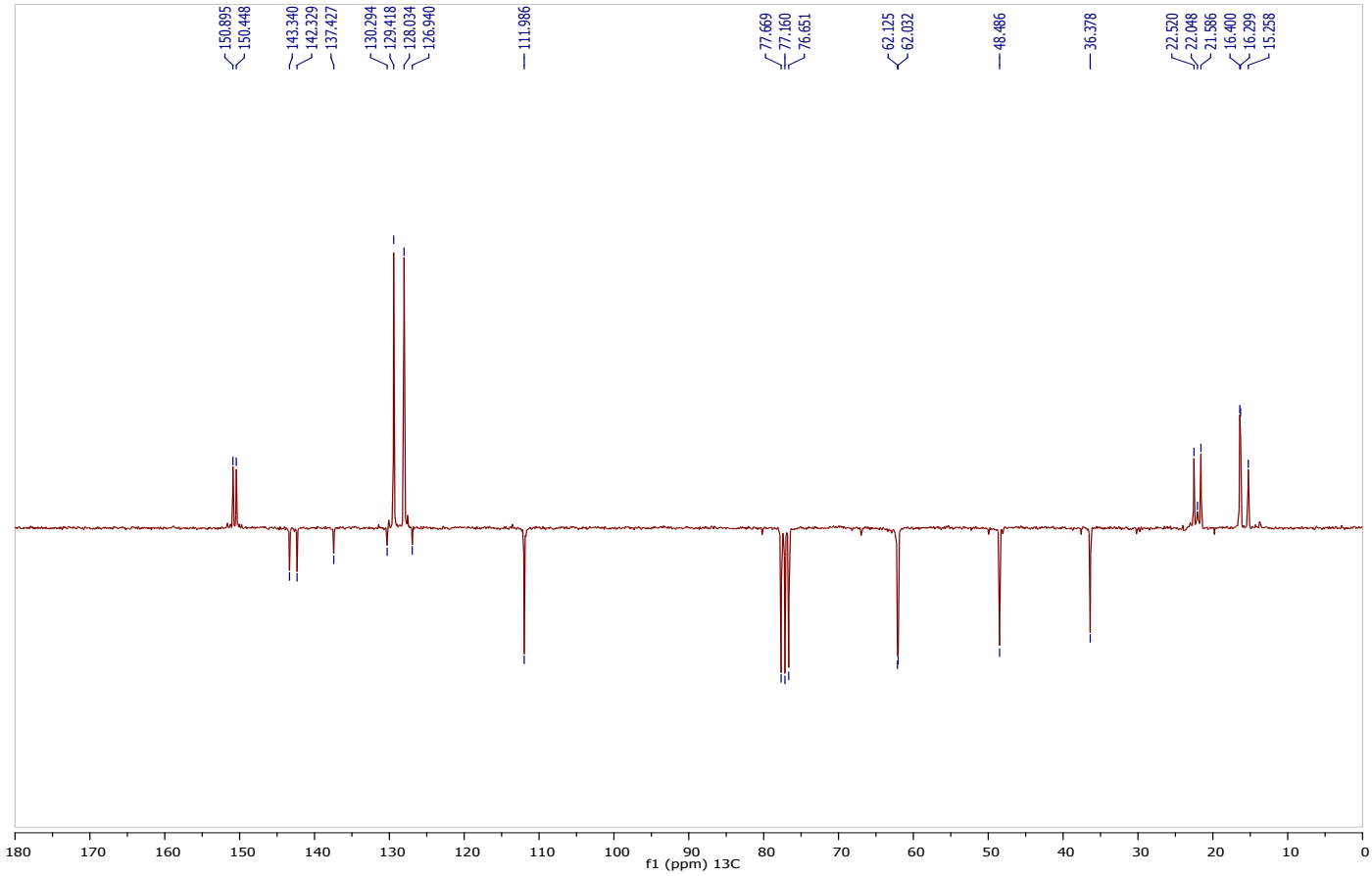
» ^{13}C NMR – 91 MHz – $CDCl_3$



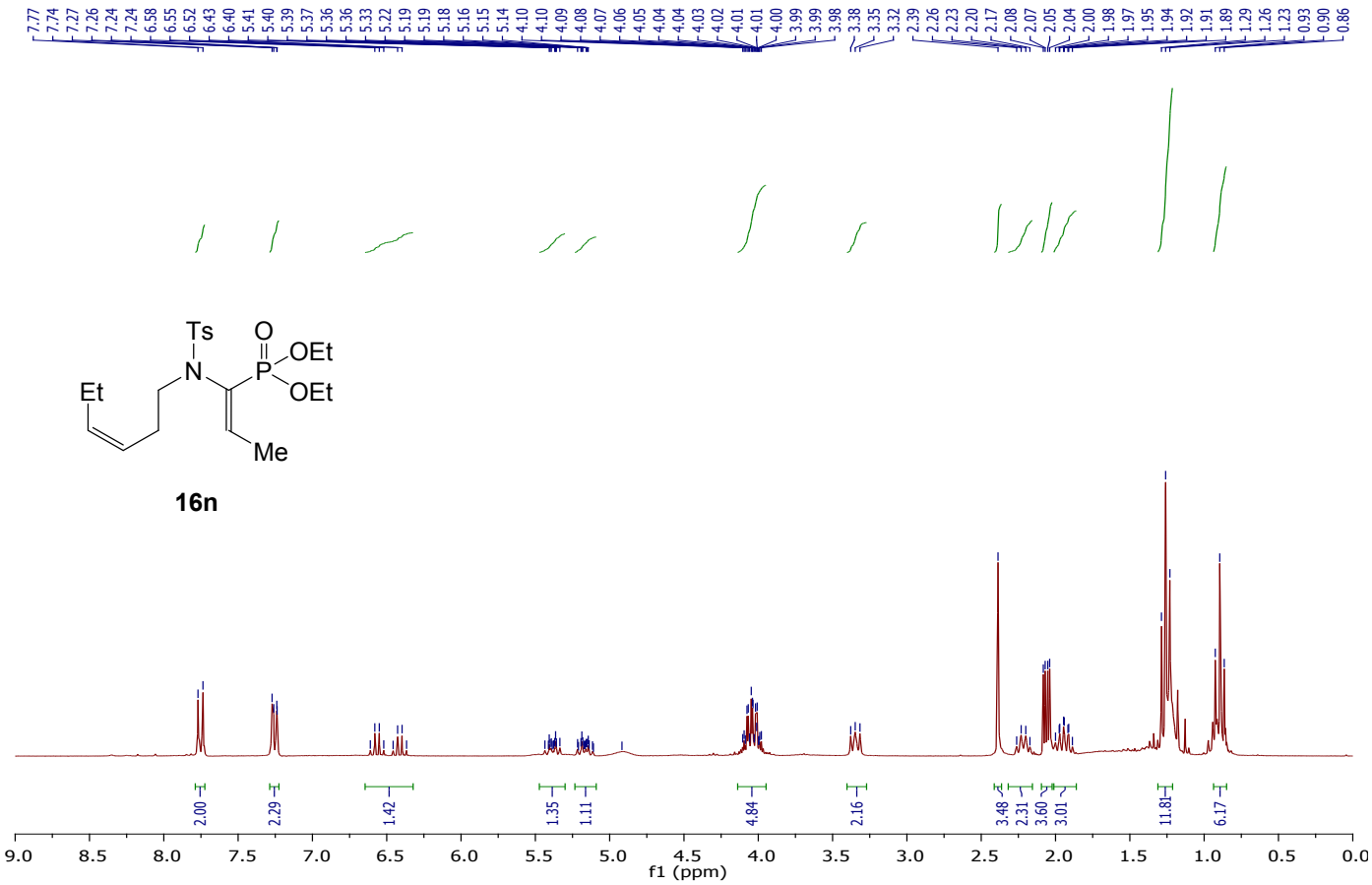
» ^{1}H NMR – 250 MHz – $CDCl_3$



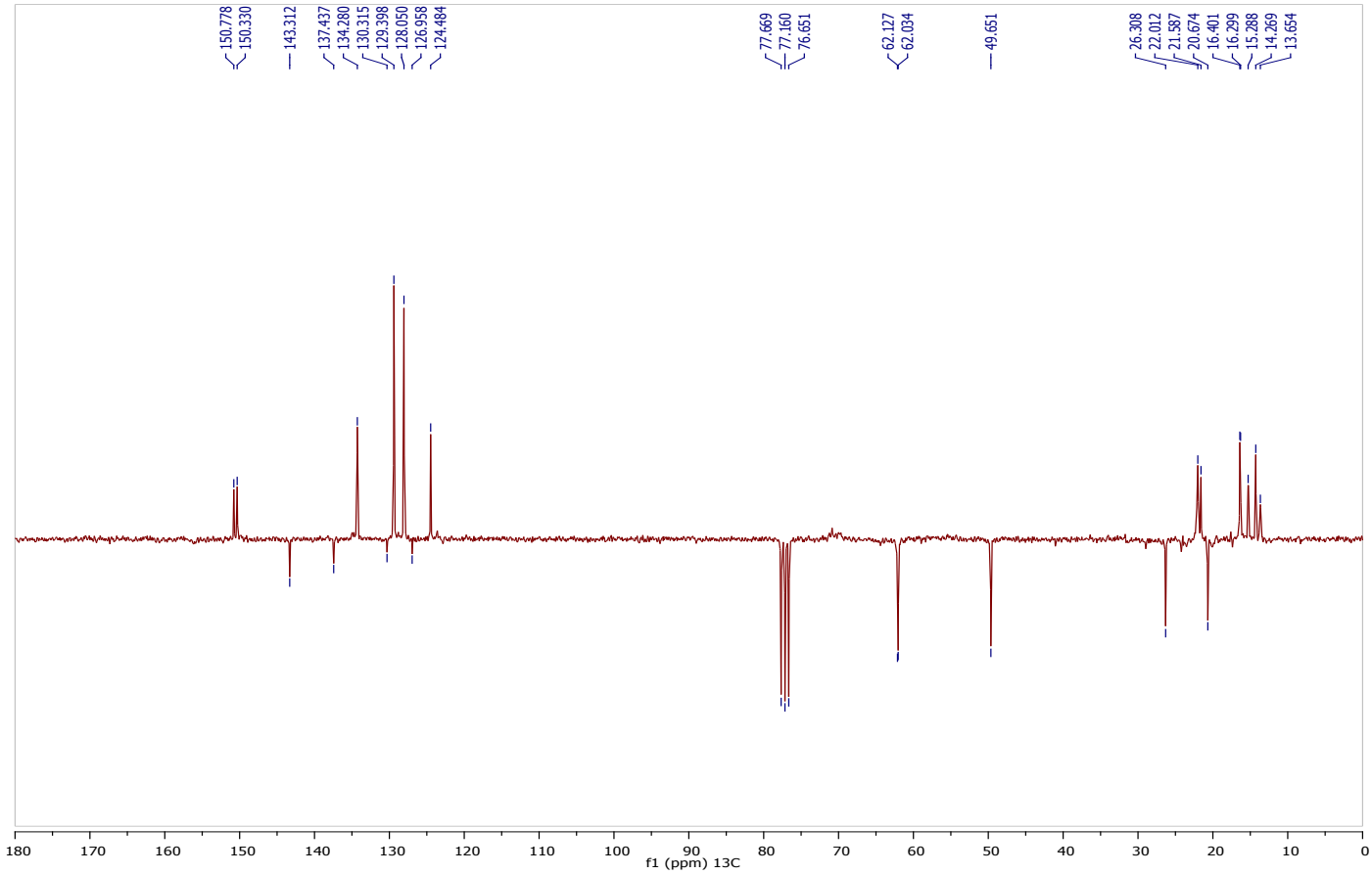
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



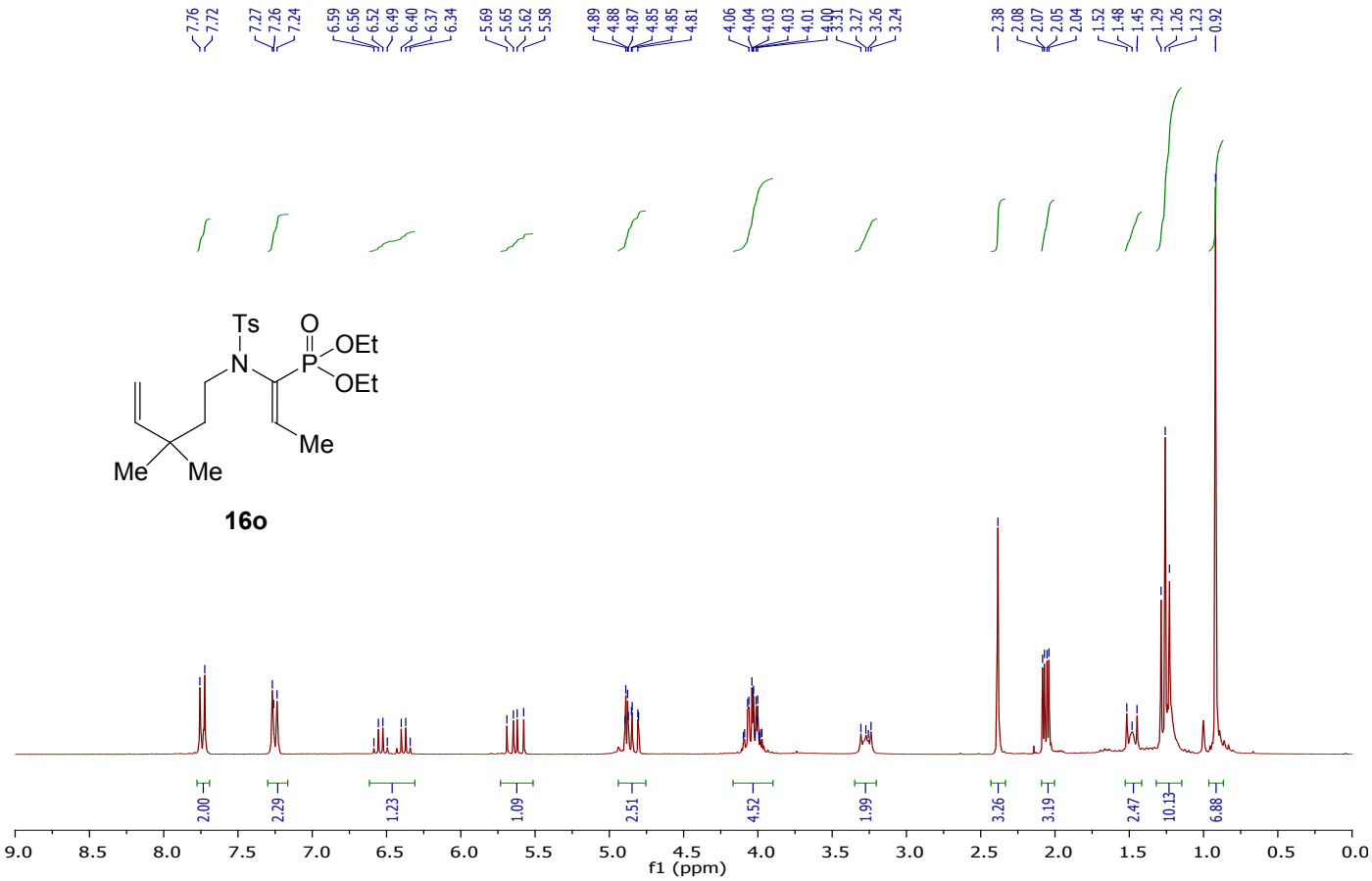
» ^{1}H NMR – 250 MHz – $CDCl_3$



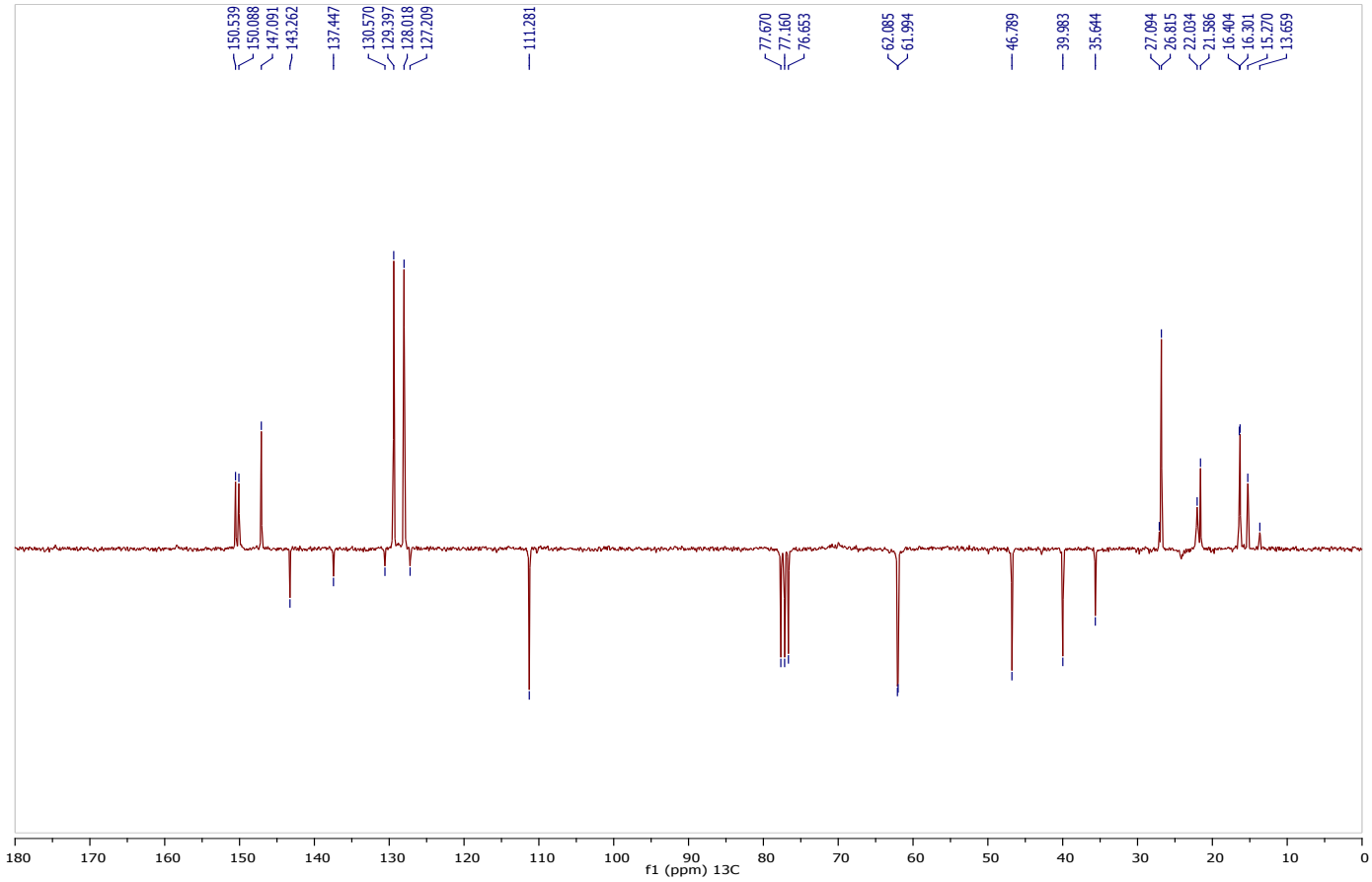
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



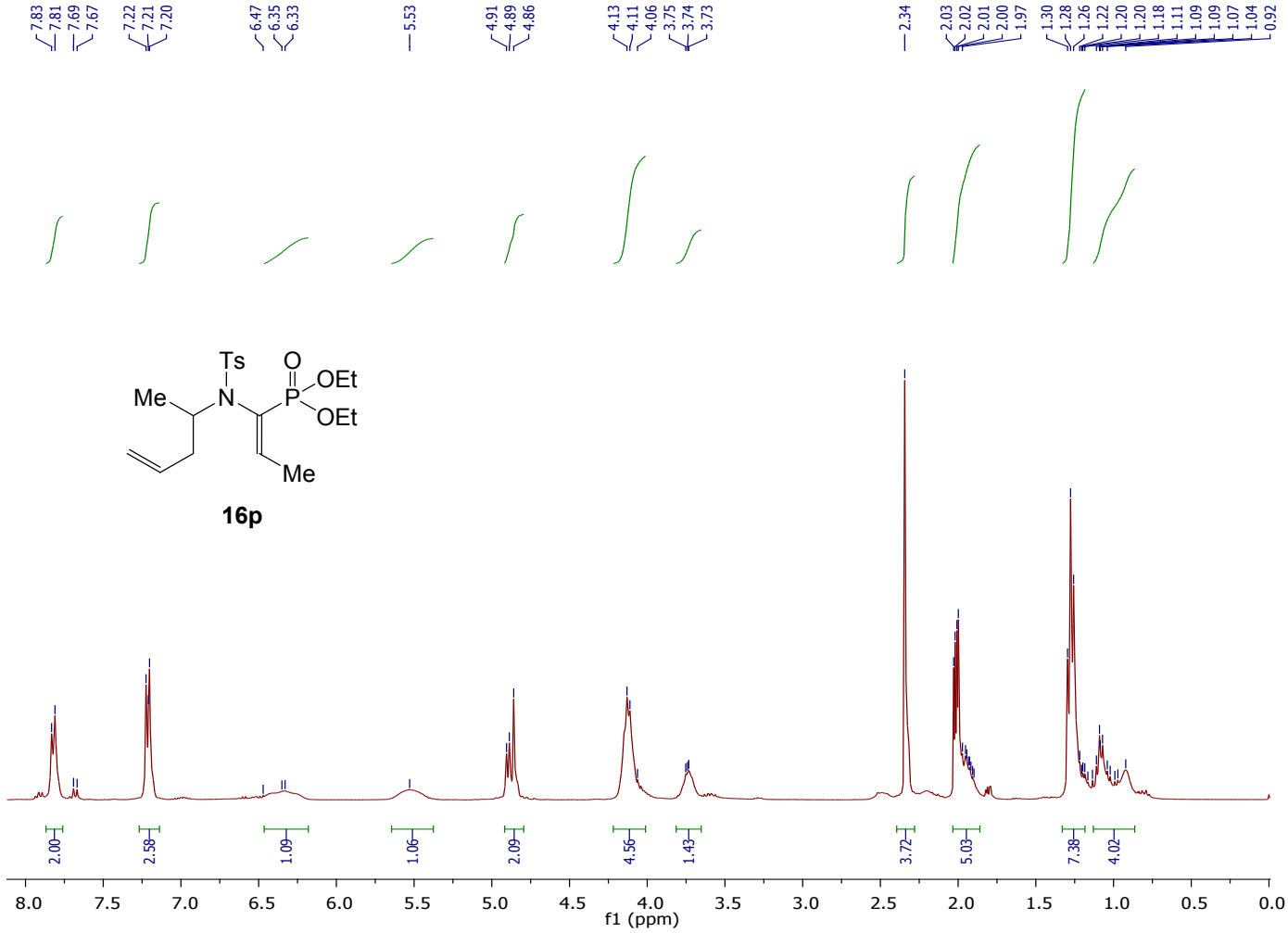
» ^{1}H NMR – 250 MHz – $CDCl_3$



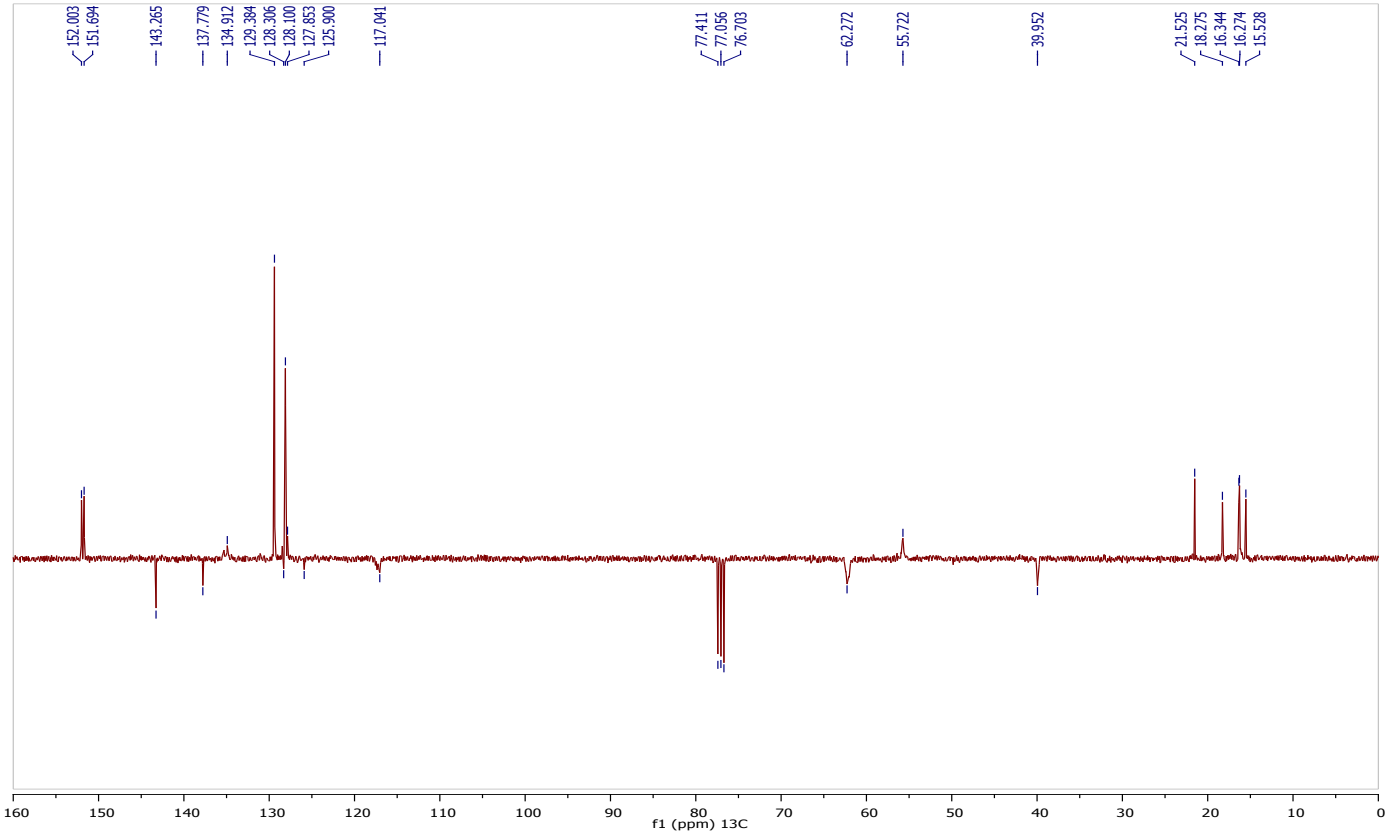
» ^{13}C NMR – 62.9 MHz – $CDCl_3$



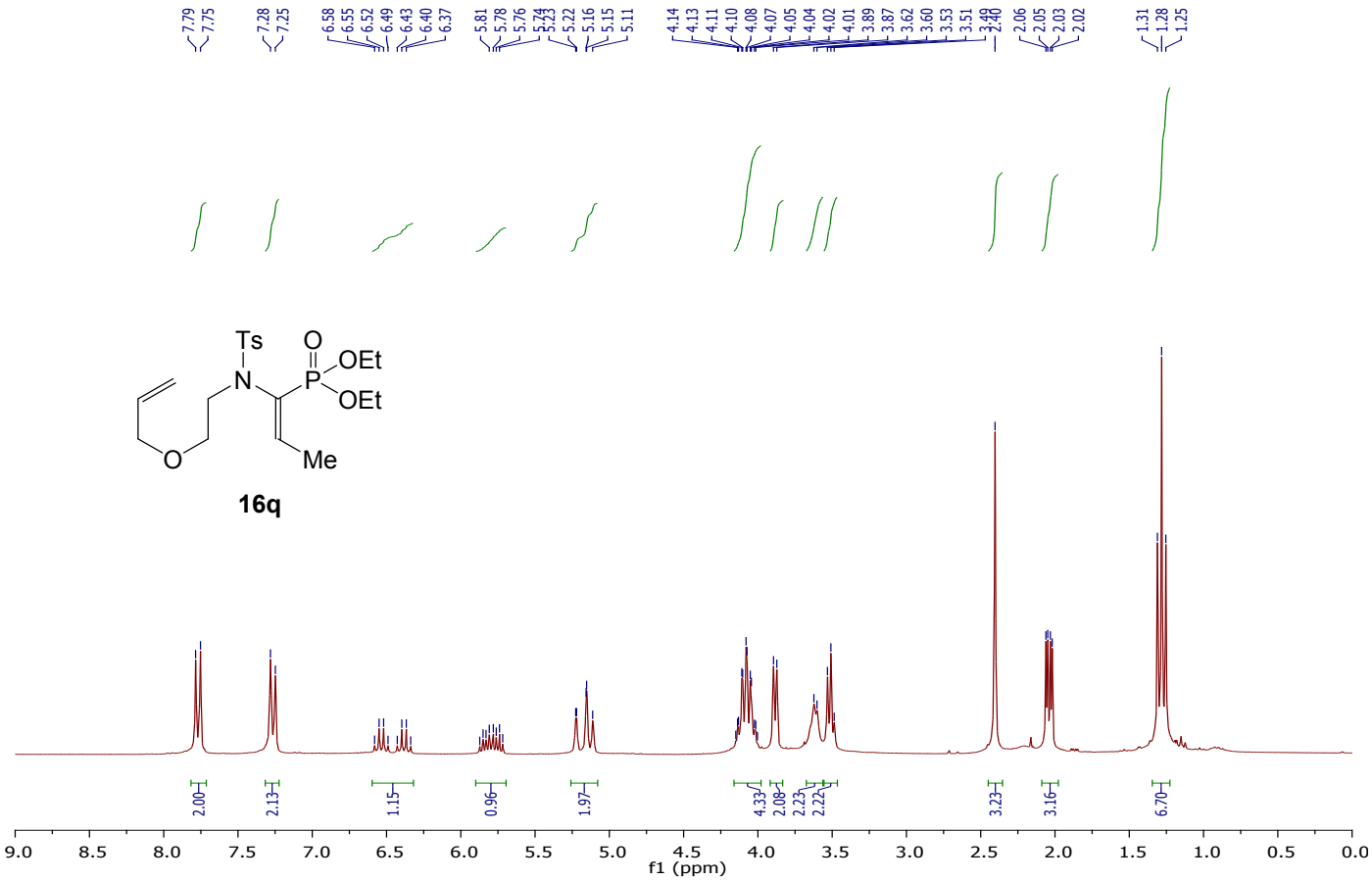
» ^{1}H NMR – 360 MHz – $CDCl_3$



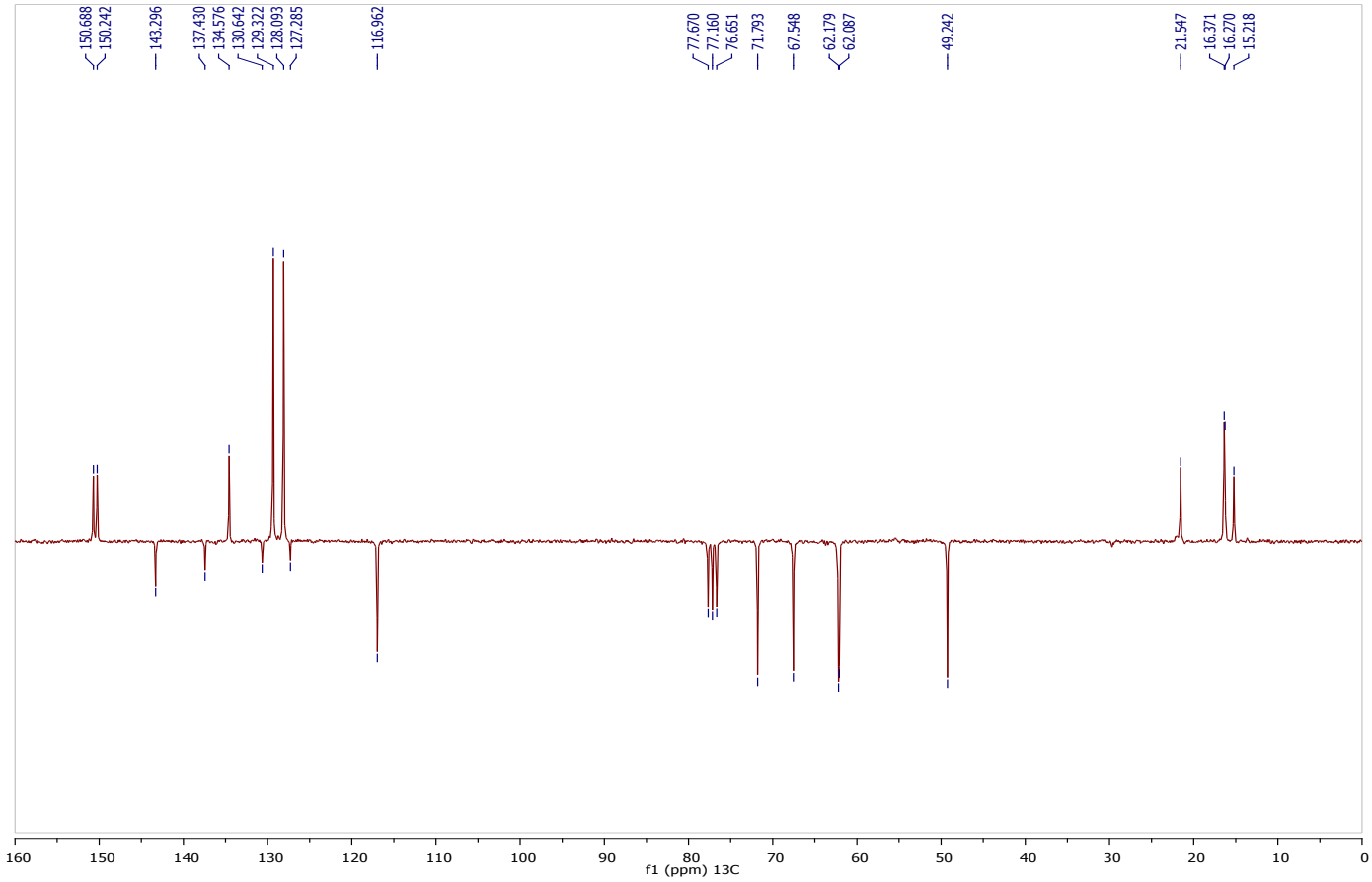
» ^{13}C NMR – 91 MHz – $CDCl_3$



» ^{1}H NMR – 250 MHz – $CDCl_3$

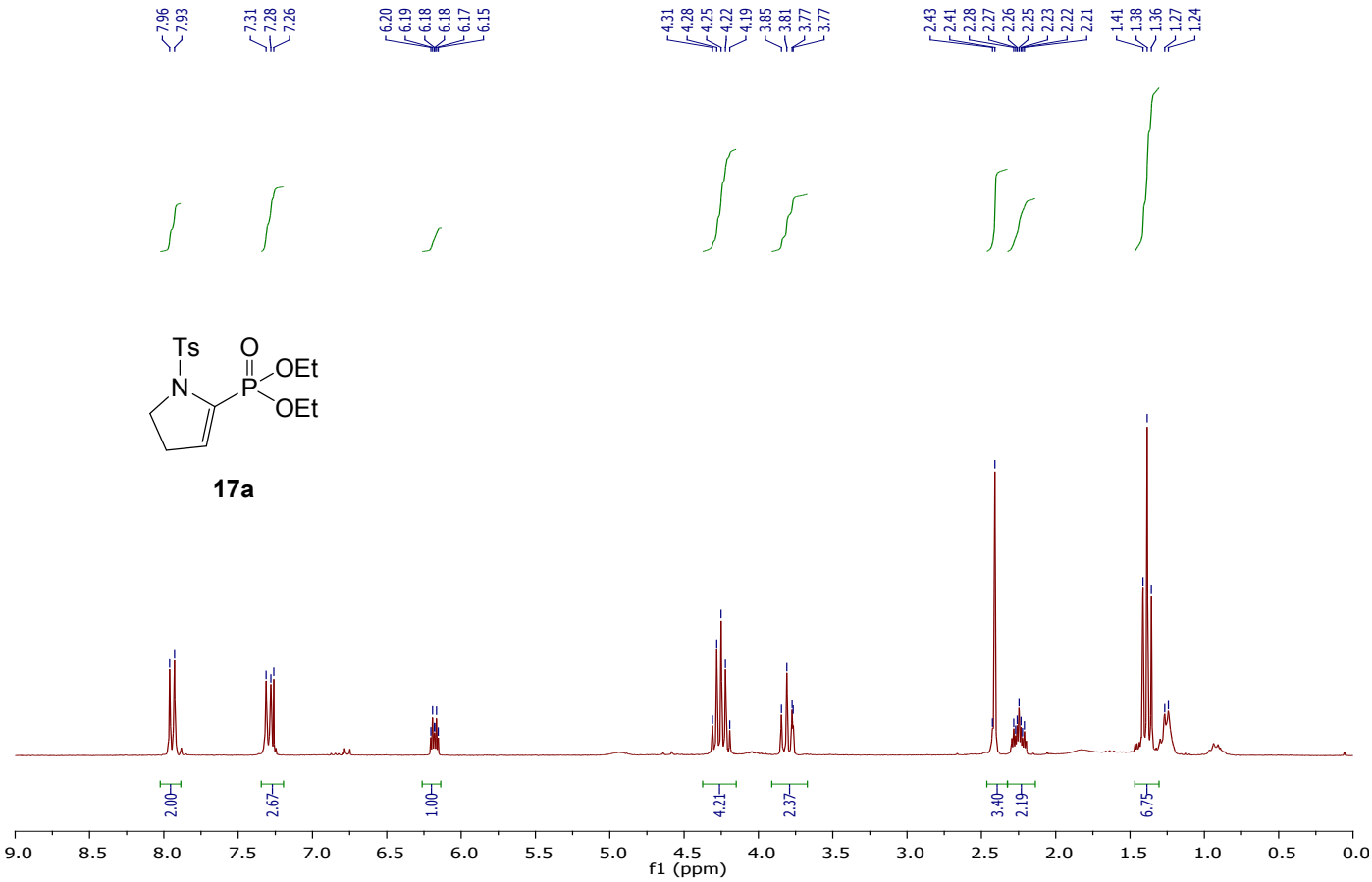


» ^{13}C NMR – 62.9 MHz – $CDCl_3$

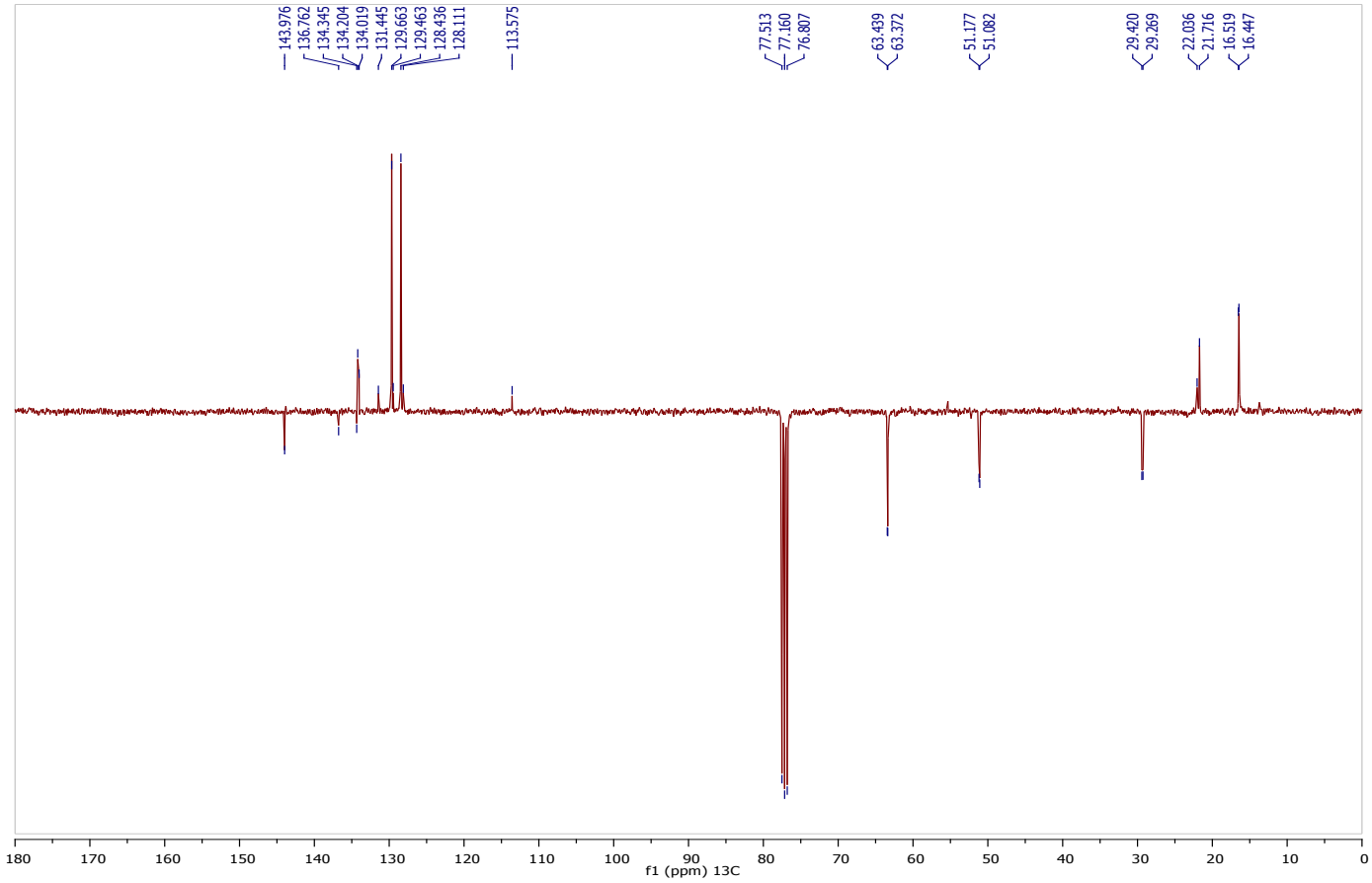


SPECTRA OF THE PRODUCTS OF METATHESIS

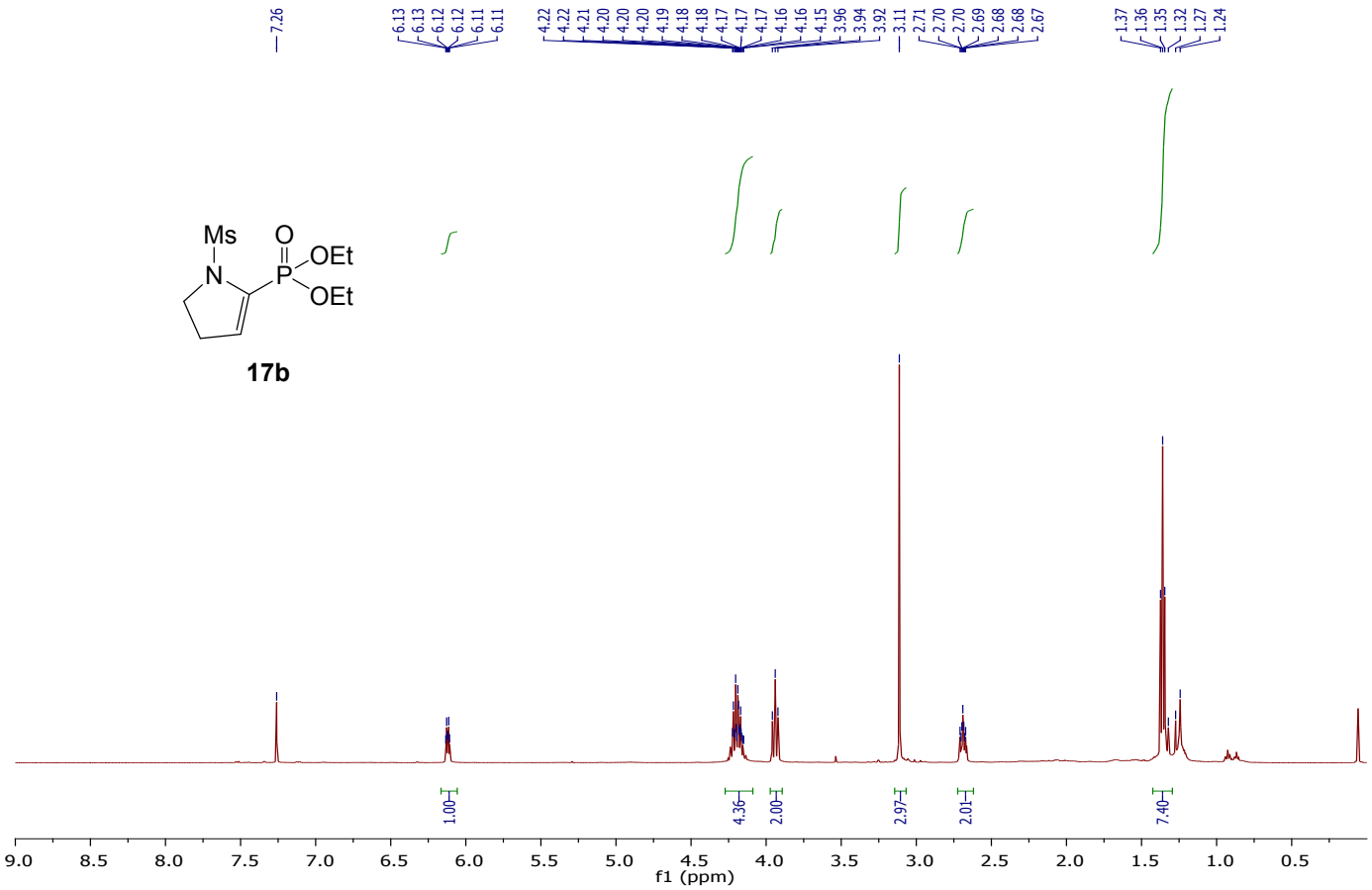
» ^{1}H NMR – 400 MHz – $CDCl_3$



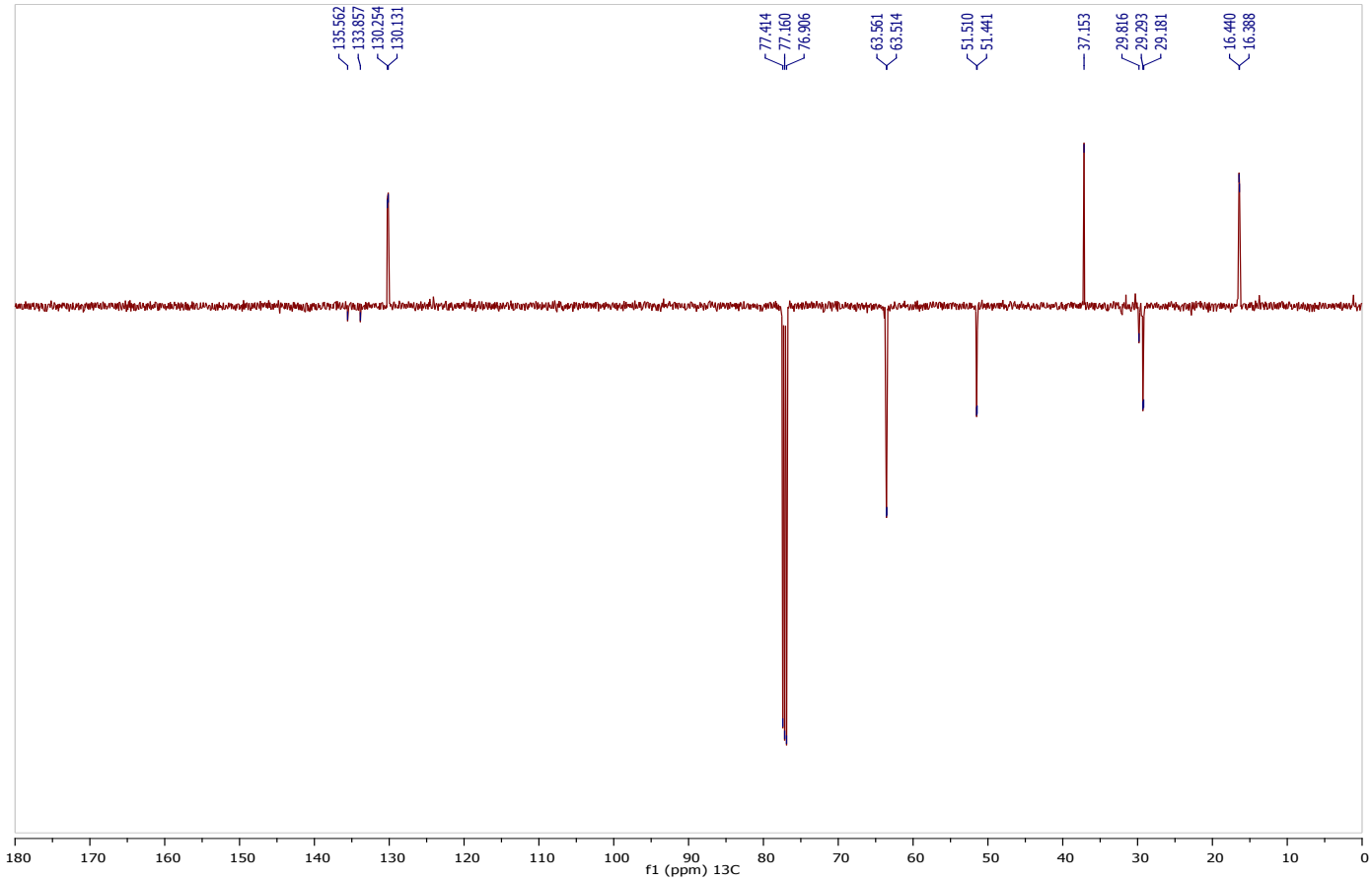
» ^{13}C NMR – 91 MHz – $CDCl_3$



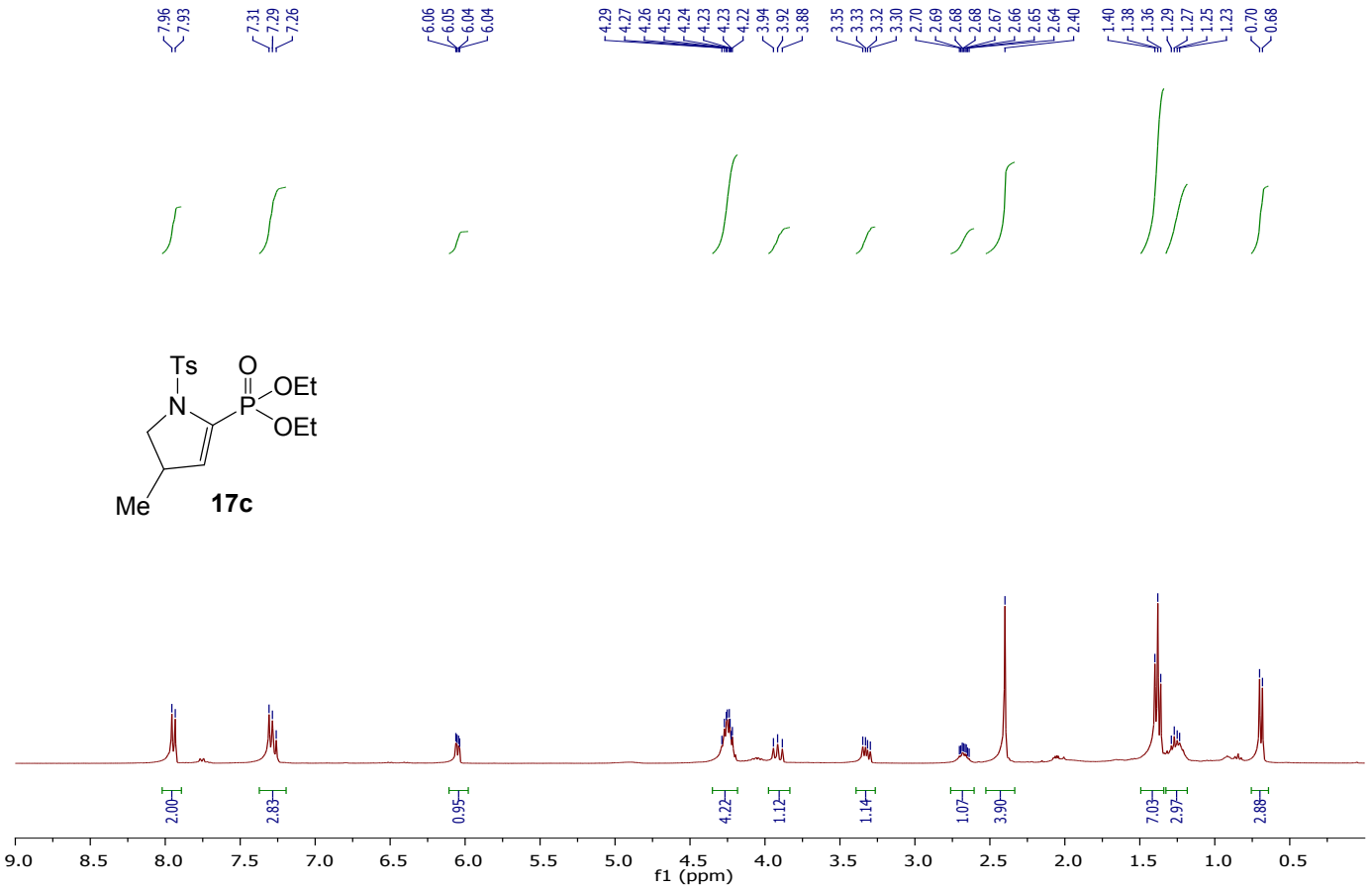
» ^{1}H NMR – 400 MHz – $CDCl_3$



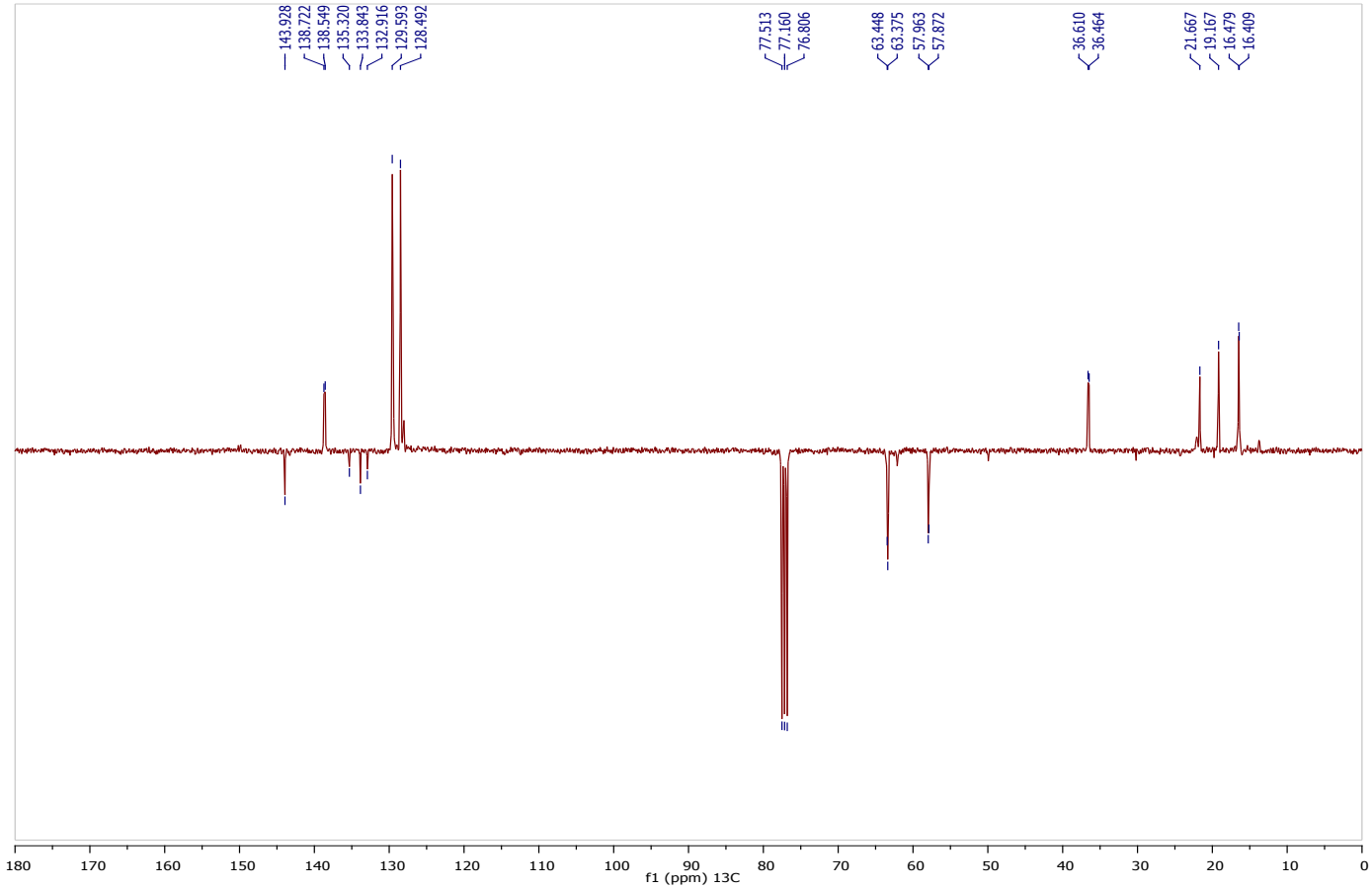
» ^{13}C NMR – 126 MHz – $CDCl_3$



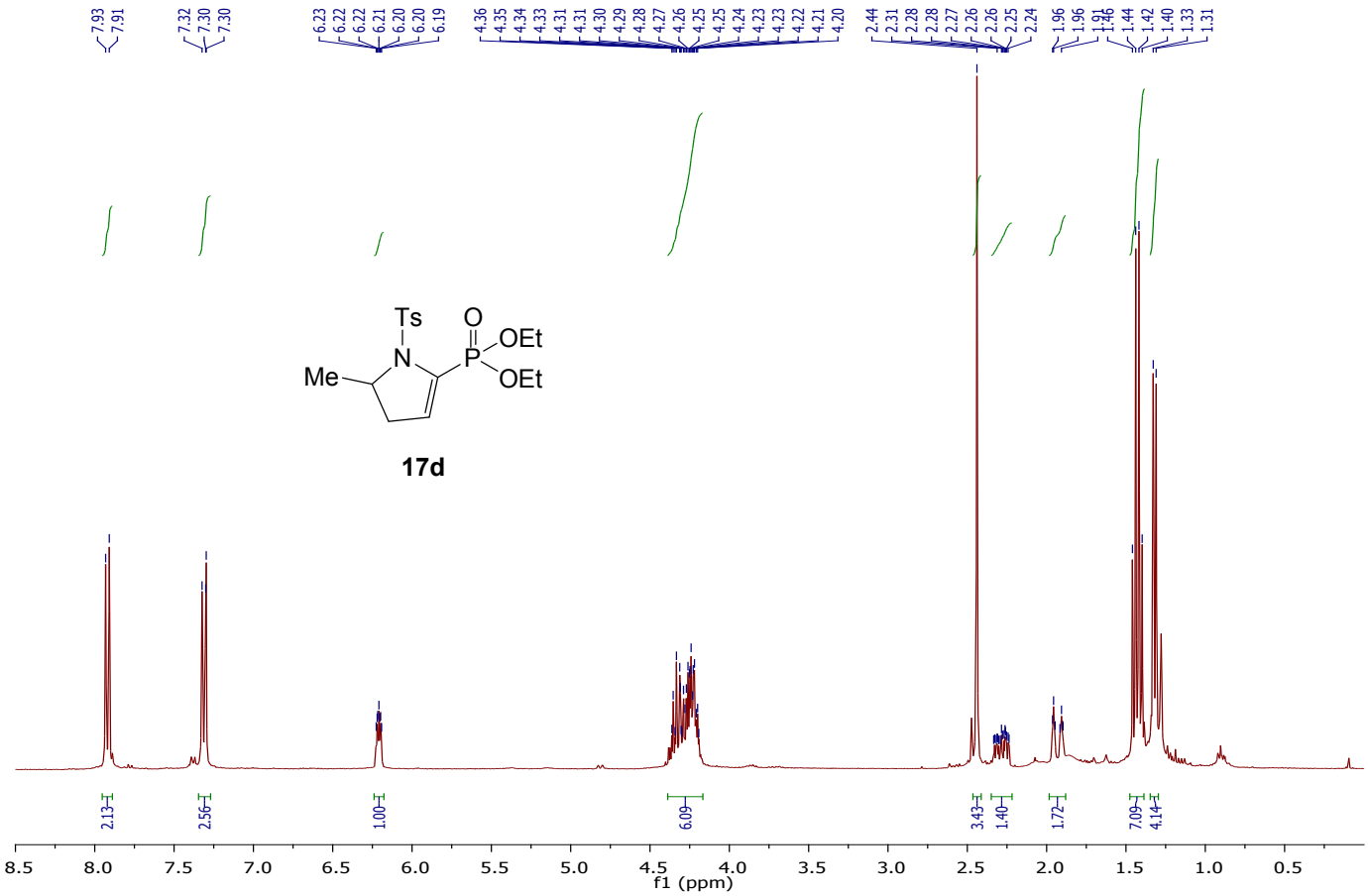
» **^{1}H NMR – 360 MHz – $CDCl_3$**



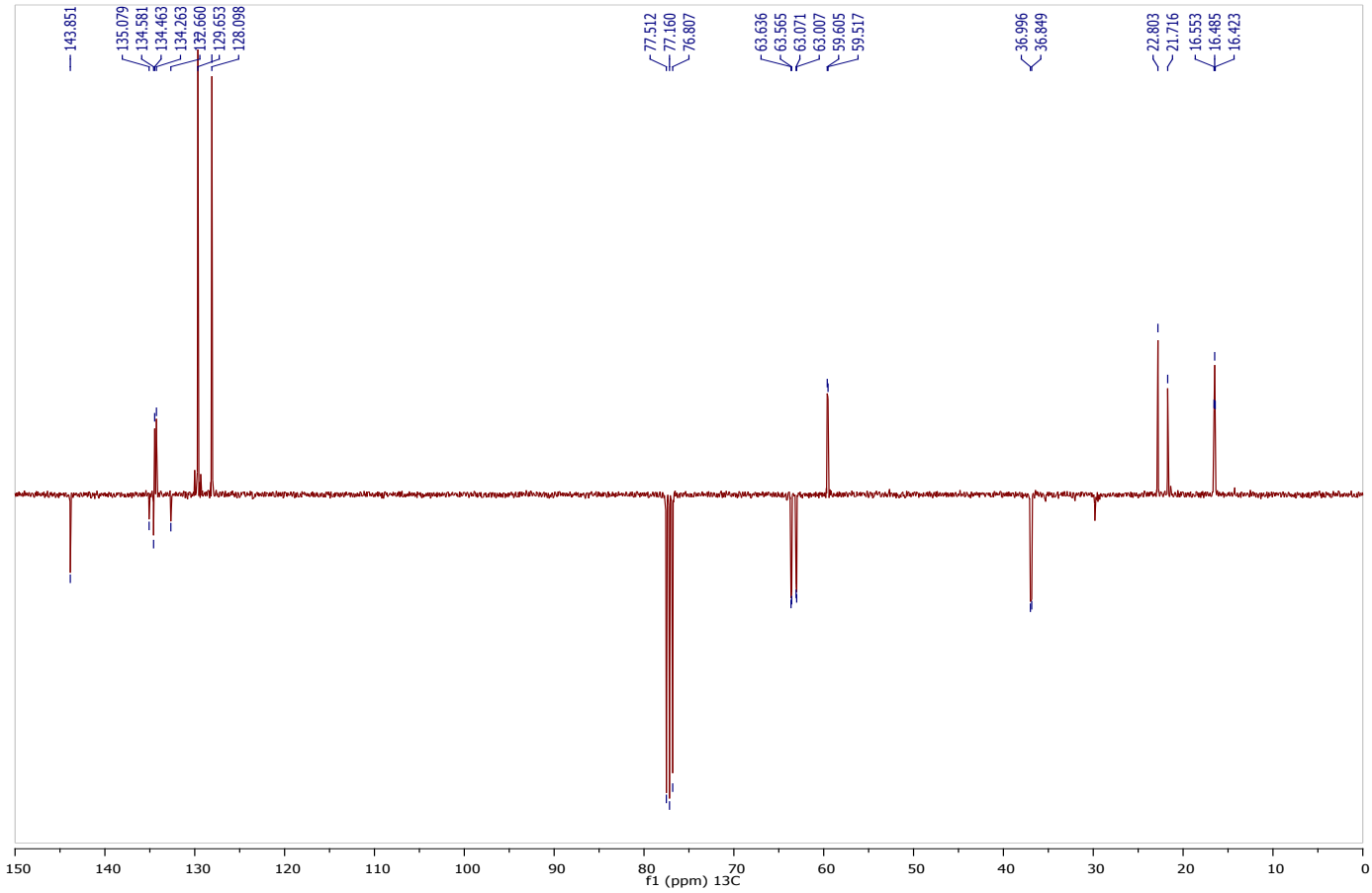
» **^{13}C NMR – 91 MHz – $CDCl_3$**



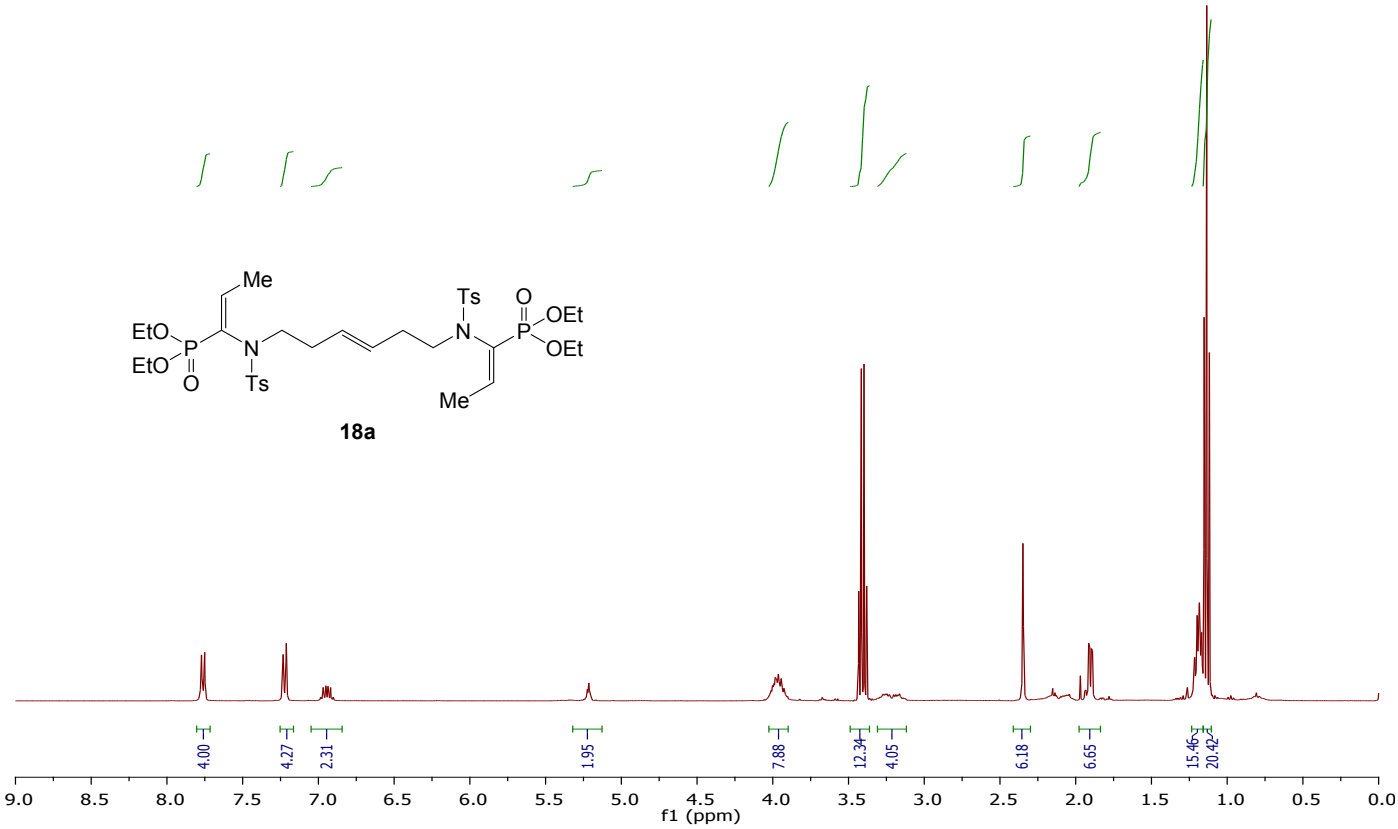
» ^{1}H NMR – 360 MHz – $CDCl_3$



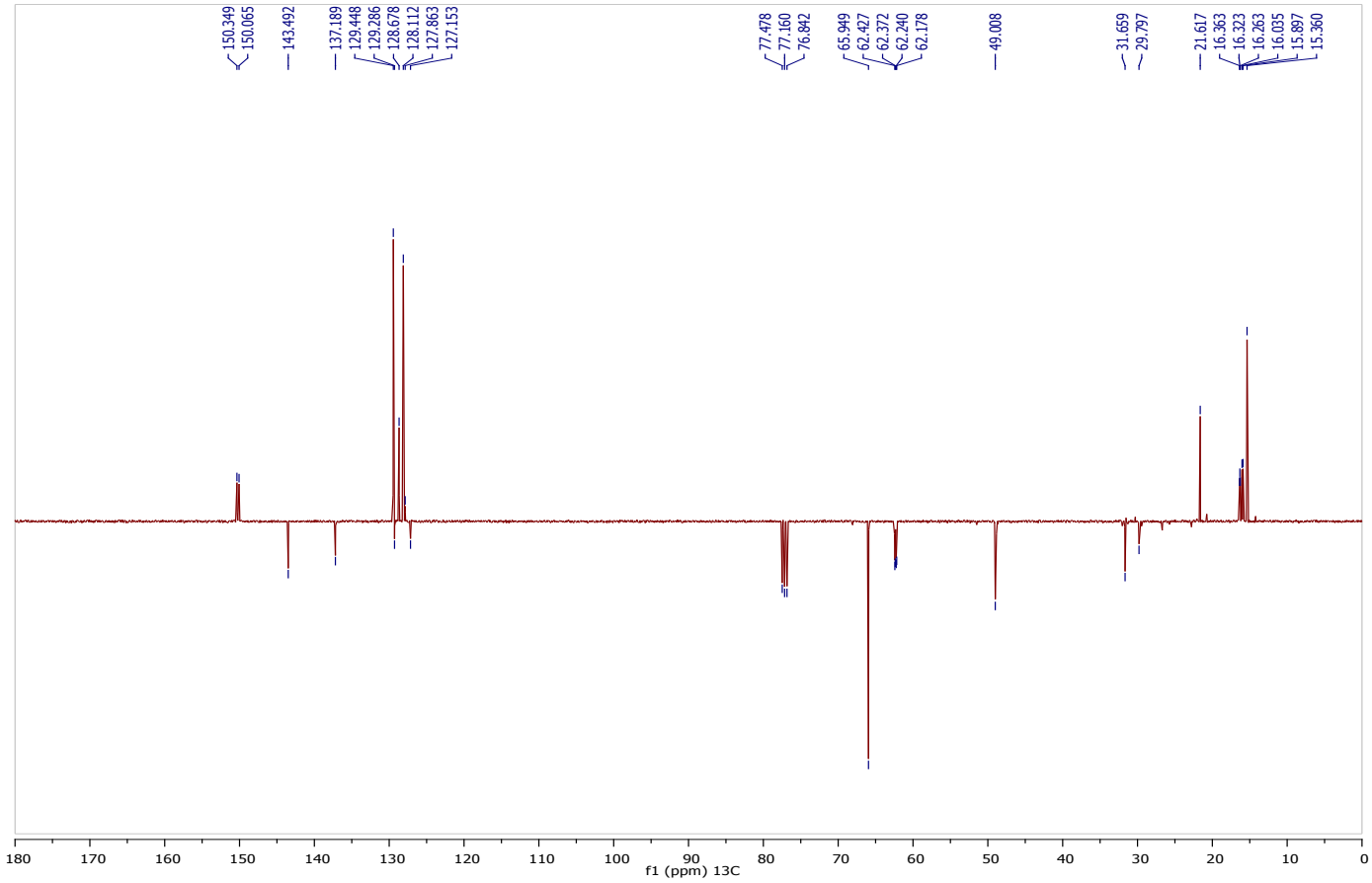
» ^{13}C NMR – 91 MHz – $CDCl_3$



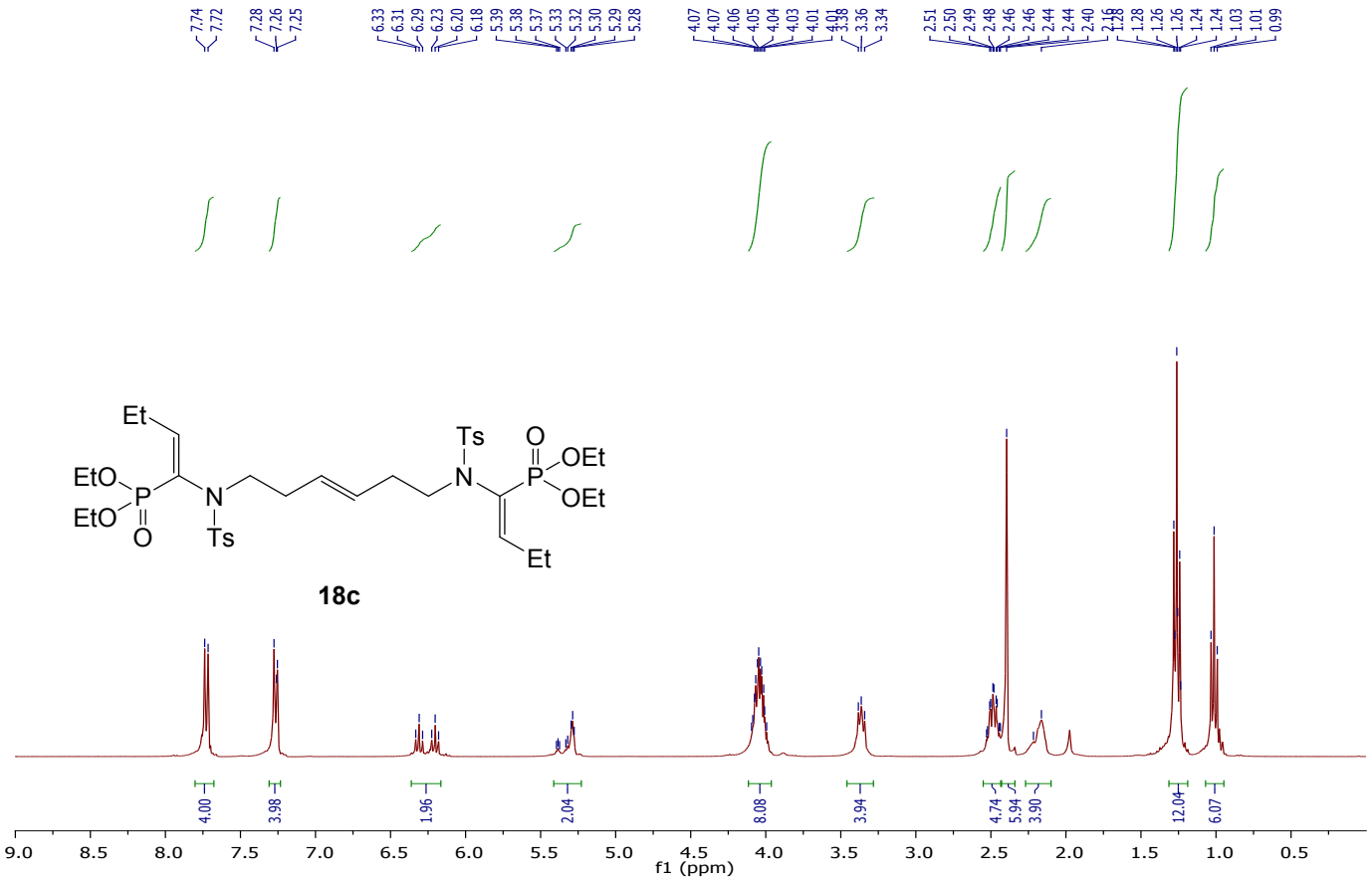
» ^{1}H NMR – 400 MHz – $CDCl_3$



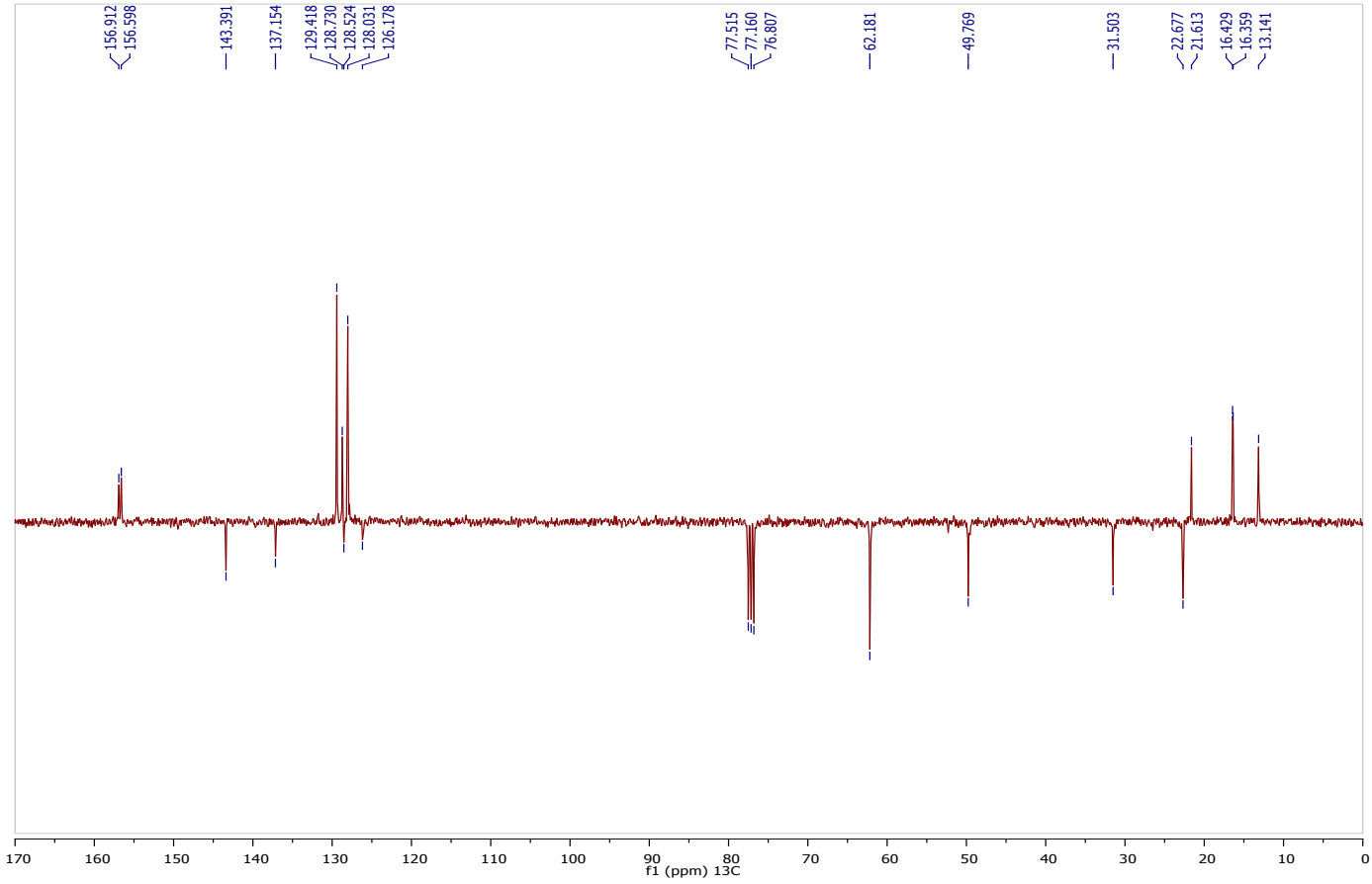
» ^{13}C NMR – 101 MHz – $CDCl_3$



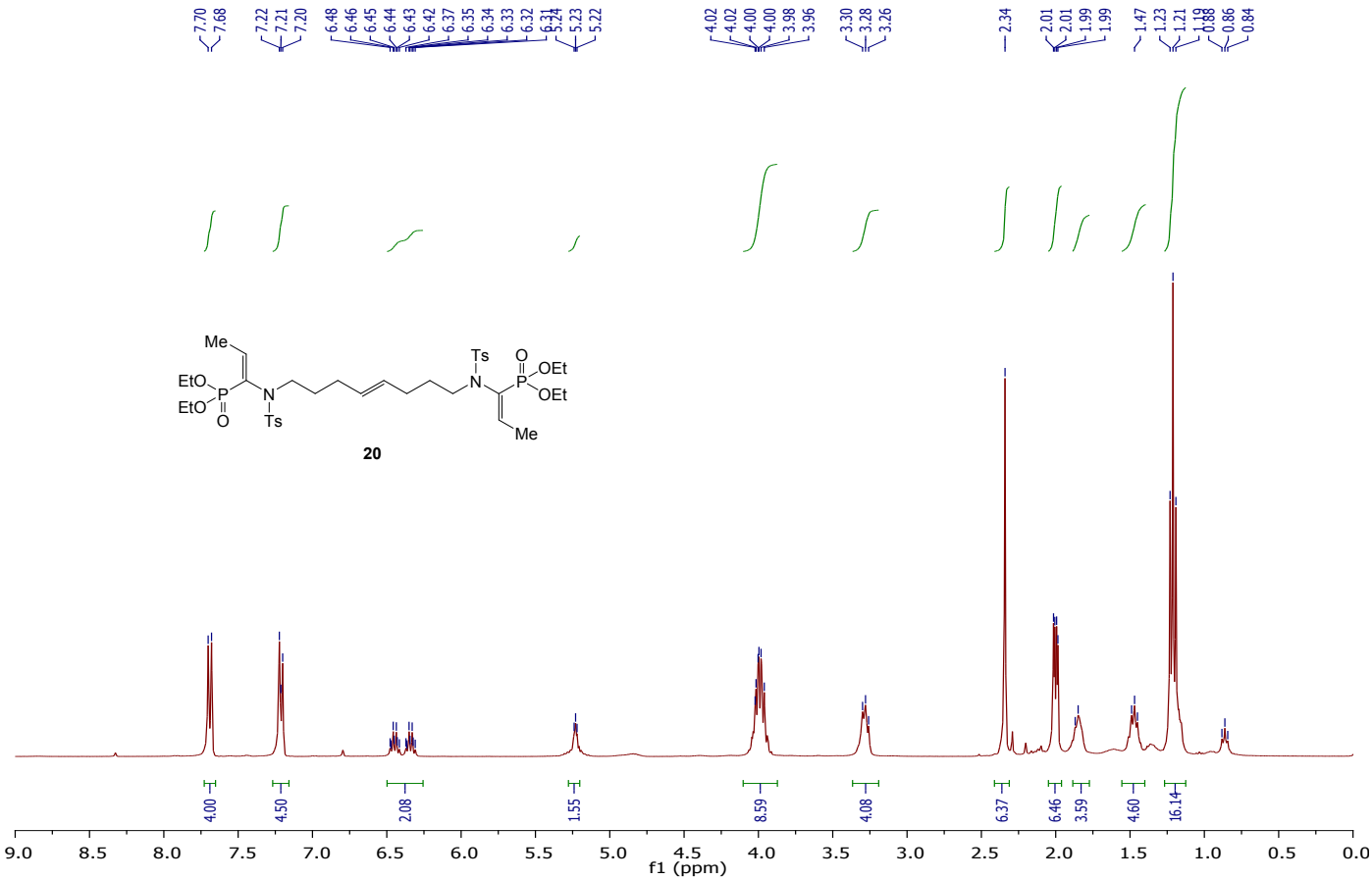
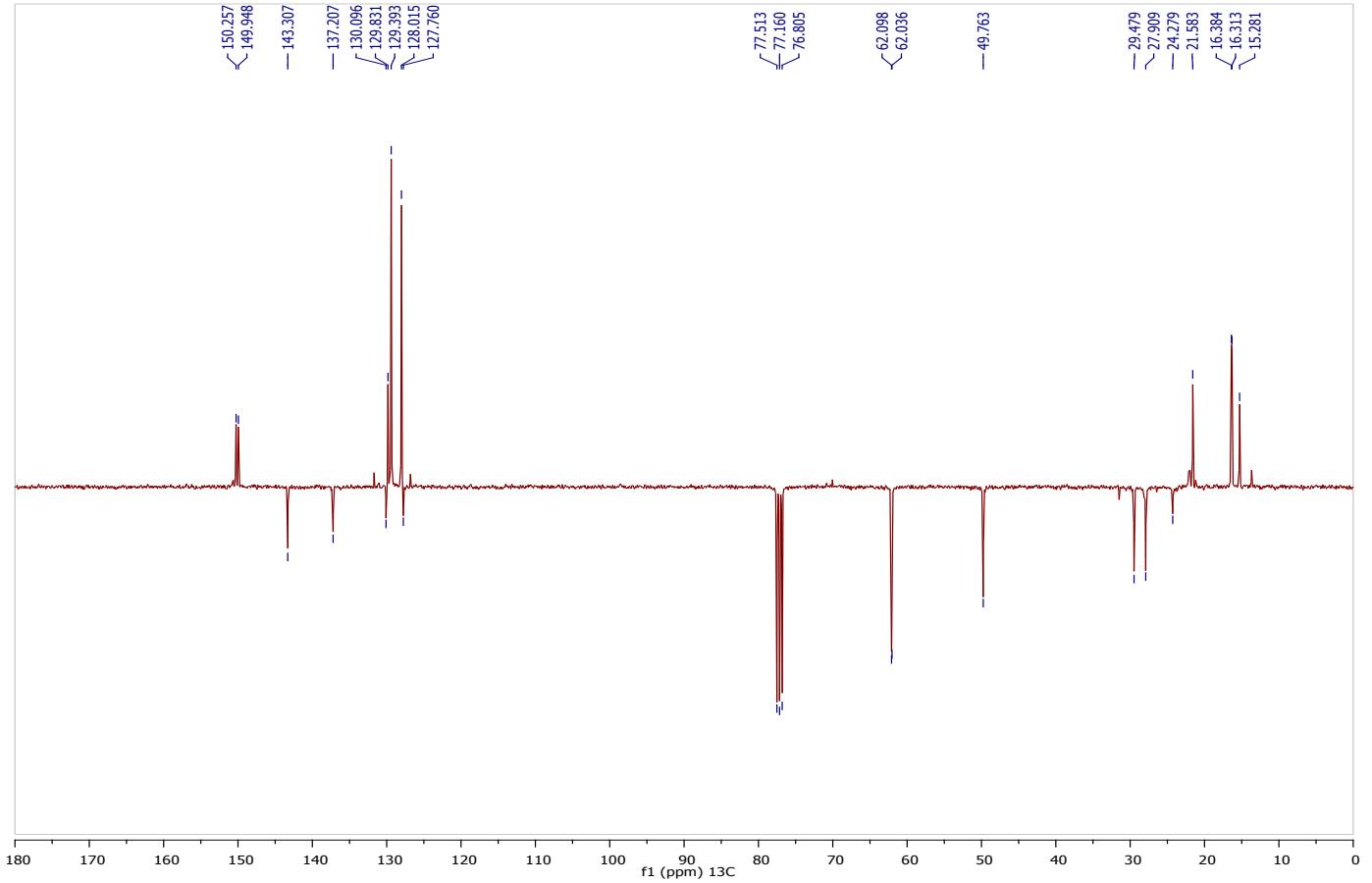
» ^{1}H NMR – 360 MHz – $CDCl_3$



» ^{13}C NMR – 91 MHz – $CDCl_3$



» ^{1}H NMR – 360 MHz – $CDCl_3$



» ^{13}C NMR – 91 MHz – $CDCl_3$